Archives of Neurology and Psychiatry

VOLUME 33 APRIL 1935 NUMBER 4

CORTICOSPINAL FIBERS ARISING IN THE PREMOTOR AREA OF THE MONKEY

DISTRIBUTION OF BOUTON TERMINATIONS

E. C. HOFF, PH.D.*

NEW HAVEN, CONN.

Though many experimental and clinical studies [1] have recently been made on the premotor area (area 6), little is known concerning its anatomic connections. Kennard [2] has shown that lesions restricted to that region of the cortex of the monkey give rise to spinal degenerations demonstrable by the Marchi method. Since premotor corticospinal

* Alexander Brown Coxe Memorial Fellow, 1933-1934.

From the Laboratory of Physiology, Yale University School of Medicine.

The material included in this article formed a part of a communication by J. F. Fulton, E. C. Hoff and Margaret A. Kennard read at the Sixtieth Annual Meeting of the American Neurological Association at Atlantic City, N. J., June 4, 1934, under the title, "The Distribution of Corticospinal Fibers from the Premotor Area as Shown by the *Boutons Terminaux* and Marchi Techniques."

1. (*a*) Brodmann, K.: Vergleichende Lokalisationslehre der Grosshirnrinde, ed. 2, Leipzig, Johann Ambrosius Barth, 1925. (*b*) Foerster, O.: The Cerebral Cortex in Man, Lancet **2**:309 (Aug. 8) 1931. (*c*) Richter, C. P., and Hines, Marion: Experimental Production of the Grasp Reflex in Adult Monkeys by Lesions of the Frontal Lobes, Am. J. Physiol. **101**:87 (Sept.) 1932. (*d*) Fulton, J. F.; Jacobsen, C. F., and Kennard, Margaret A.: A Note Concerning the Relation of the Frontal Lobes to Posture and Forced Grasping in Monkeys, Brain **55**: 524 (Dec.) 1932. (*e*) Fulton, J. F., and Kennard, Margaret A.: The Relation of the Motor and Premotor Areas of the Cortex to Spasticity and Postural Reflexes in Primates, Am. J. Physiol. **105**:35 (July) 1933. (*f*) Fulton, J. F.: Forced Grasping and Groping in Relation to the Syndrome of the Premotor Area, Arch. Neurol. & Psychiat. **31**:221 (Feb.) 1934. (*g*) Vogt, Cécile, and Vogt, O.: Allgemeinere Ergebnisse unserer Hirnforschung, J. f. Psychol. u. Neurol. **25**:276, 1919. (*h*) Bucy, P. C.: Electrical Excitability and Cyto-Architecture of the Premotor Cortex in Monkeys, Arch. Neurol & Psychiat. **30**:1205 (Dec.) 1933. (*i*) Bucy, P. C., and Fulton, J. F.: Ipsilateral Representation in the Motor and Premotor Cortex of Monkeys, Brain **56**:318 (Sept.) 1933. (*j*) Fulton, J. F.; Kennard, Margaret A., and Watts, J. W.: Autonomic Representation in the Cerebral Cortex, Am. J. Physiol., to be published. (*k*) Watts, J. W., and Fulton, J. F.: Intussusception: Relation of the Cerebral Cortex to Intestinal Motility in the Monkey, New England J. Med. **210**:883 (April 26) 1934. (*l*) Bucy, P .C.: Electrical Excitability of the Premotor Area of the Cortex in Monkeys as Correlated with Cyto-Architecture, Am. J. Physiol. **105**:14 (July) 1933.

2. Kennard, Margaret A.: Corticospinal Fibers Arising in the Premotor Area of the Monkey as Demonstrated by the Marchi Method, Arch. Neurol. & Psychiat., p. 698.

fibers descend through the brain and brain stem along with the pyramidal fibers, it becomes a problem of importance to know where and how these fibers end in the spinal cord. The *bouton* method, previously used for studying terminations of the pyramidal tracts [3] and posterior root fibers,[4] has been utilized, since it allows an estimation of the proportion of ipsilateral to contralateral fibers, as well as a determination of the individual neurons on which each fiber terminates.

PROCEDURES

The bouton method is based on the observation that severing axons from their cell bodies results in an early disintegration of the *boutons terminaux* which are the end-organs by which these axons make synaptic contacts with other neurons. After section of dorsal roots in cats [4] and monkeys,[5] many *boutons terminaux* surrounding spinal neurons show a progressive swelling and granulation, recognizable as early as from twenty-four to forty hours after production of the lesions, reaching a climax in three days and followed by a complete destruction of the terminals in from four to six days. The course and time relations of this degeneration of the *boutons* are the same whether the axons sectioned are short, like the locally terminating collaterals of dorsal root fibers, or whether they are long projection fibers from the cerebral cortex or brain stem. It is therefore possible to trace the terminal distribution of fibers by plotting the occurrence of degenerated *boutons terminaux* around nerve cells in animals killed three days after lesions involving the fiber tract or area to be studied. The method of *bouton* degeneration has been previously used in determining the terminal distribution of corticospinal fibers from the motor cortex in cats [3a] and monkeys [3b] and has been applied in the present experiments to study the endings of projection fibers originating in the premotor area.

Premotor lesions have been made in five monkeys (*Macaca mulatta*) with subsequent examination of degeneration of *boutons terminaux;* in two monkeys the entire area 6 was removed at one operation; in two the cortex was superficially incised between areas 4 and 6; in one a superficial cortical incision between areas 4 and 6 was followed eighteen days later by extirpation of the premotor area of the same side, and finally in a baboon in which the right and left motor and frontal areas had been ablated in four successive operations, a unilateral extirpation of area 6 was performed. Surgical procedures were carried out under aseptic conditions, using the neurosurgical technic described by Fulton and Keller.[6]

---

3. (*a*) Hoff, E. C.: The Distribution of the Spinal Terminals (*Boutons*) of the Pyramidal Tract, Determined by Experimental Degeneration, Proc. Roy. Soc., London, s.B **111**:226 (July) 1932. (*b*) Hoff, E. C., and Hoff, H. E.: The Spinal Terminations of Projection Fibers from the Motor Cortex in Monkeys, Brain, to be published.

4. Hoff, E. C.: Central Nerve Terminals in the Mammalian Spinal Cord and Their Examination by Experimental Degeneration, Proc. Roy. Soc., London, s.B **111**:175 (July) 1932.

5. Hoff, E. C.: Unpublished data, 1933.

6. Fulton, J. F., and Keller, A. D.: The Sign of Babinski, Springfield, Ill., Charles C. Thomas, Publisher, 1932.

Neurologic examinations of the animals were made in all the experiments, and whenever possible the excitability of the cortex was determined by electrical stimulation under ether anesthesia just before death. Under ether anesthesia the animals were then exsanguinated by the injection of 0.9 per cent saline solution into the abdominal aorta. When clear fluid flowed from the opened inferior vena cava 500 to 1000 cc. of a 10 per cent solution of chloral hydrate was introduced, and the brain and cord were removed immediately. Histologic preparations of the cortex, brain stem, medulla and cord were made by Cajal's reduced silver impregnation method,[7] and all the pieces of extirpated cortical tissue were stained by the Nissl technic. The location of the cortical incisions was confirmed by histologic sections prepared either by silver impregnation or by the Nissl method.

OBSERVATIONS

The observations and conclusions rest on evidence drawn from three groups of experiments, as follows: (1) primary extirpation of the premotor area, (2) superficial incision of the cortex between areas 4 and 6 and (3) removal of the premotor area after destruction and degeneration of its fiber connections with other cortical regions of the frontal lobe. The following protocols illustrate the results obtained.

Primary Extirpation of the Premotor Area.—EXPERIMENT 1 (pyramidal *bouton* series, no. 5).—The left premotor area was extirpated from a young rhesus monkey (March 27, 1934), and the extirpated tissue was placed immediately in 95 per cent alcohol to be stained by the Nissl technic. The extent of the area removed is shown in figure 1. After the operation the animal exhibited well-marked forced grasping of the right upper extremity throughout the postoperative period.

The animal was killed under deep anesthesia on March 30, 1934. The cortex was exposed, and bipolar faradic stimulation evoked brisk sustained responses from both motor areas and isolated as well as complex movements of the contralateral extremities from the right premotor area. The crater of the lesion in the left hemisphere was completely inexcitable even with very strong stimuli.

Following the injection of chloral hydrate the brain and cord were immediately removed and sections prepared by the Cajal method.

Histologic Observations of the Extirpated Area: Nissl sections of the block removed at autopsy showed that there had been no involvement of the Betz cell area.

Distribution of Degenerated *Boutons* Within the Spinal Cord (figs. 2 and 8): At all the levels of the cord typical degenerated *boutons terminaux* occurred predominantly around cells at the base of the dorsal and ventral horns in the gray matter of the contralateral side, with a scattering of degenerated terminals in the ventral horn. On the ipsilateral side degenerated endings were distributed in a region corresponding to the contralateral distribution of the degenerated *boutons*, and the ratio of the numbers of such endings on the contralateral and ipsilateral sides was about 4:1.

EXPERIMENT 2 (pyramidal *bouton* series, no. 8).—On Jan. 15, 1934, the right premotor area was extirpated from a young rhesus monkey (fig. 3). After the operation the animal showed a disinclination to use the left forelimb, and well

7. Lee, B.: Microtomist's Vade-Mecum, ed. 9, Philadelphia, P. Blakiston's Son & Co., 1928. Hoff.[4]

marked forced grasping could be elicited from that limb throughout the postoperative period. The animal was killed on Jan. 19, 1934, by injection under ether anesthesia of saline solution followed by solution of chloral hydrate, and the usual Cajal preparations of the cord were made.

Histologic Observations of the Localization of the Posterior Boundary of the Lesion: Serial sections of the right precentral gyrus showed that the posterior limit of the lesion lay about 1 mm. anterior to the anterior limit of the Betz cell area.

Distribution of Degenerated *Boutons* in the Cord (fig. 4): In this cord the cells lying on the intermediate zone of the gray matter of the contralateral side

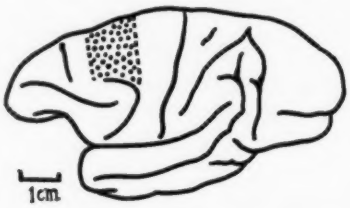


Fig. 1 (experiment 1; Macaca mulatta).—Tracing of the left cerebral hemisphere. The extirpated premotor area is indicated by black dots.

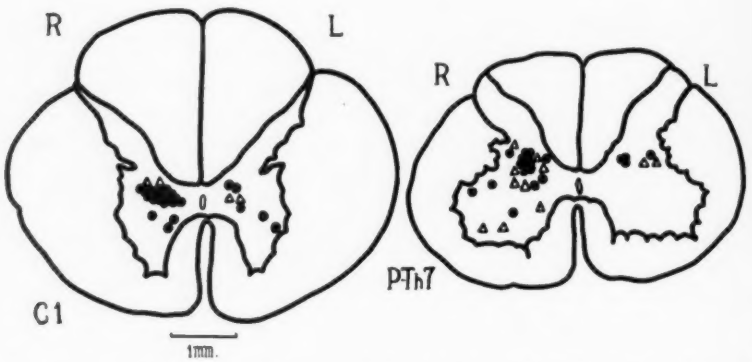


Fig. 2 (experiment 1).—Sections of the spinal cord at the levels of the first cervical and seventh postthoracic segments, showing the distribution of *bouton* degeneration in the gray matter three days after removal of the left premotor area. The black circles indicate cell bodies on which degenerated *boutons* were found; the triangles represent dendrites showing degenerated terminals. (The diagram was drawn with a projector.)

showed an extensive degeneration of *boutons*. This degeneration was most pronounced on the perikaryal surfaces but occurred also on the proximal ends of the long dendrites. In addition to this massive degeneration in the midregion, isolated degenerated *boutons terminaux* were found scattered in the dorsal part of the ventral horn; it was not possible to see any degenerated terminals around large motor neurons in the extreme ventral horn. The ipsilateral degeneration, which

was quantitatively about one-fourth that on the contralateral side, was confined to the cell bodies and dendrites of the midregion.

Superficial Incision of the Cortex Between Area 6 and Area 4.—Foerster's [1b] and Bucy's [1h] experiments indicate that sustained isolated responses from the premotor cortex are mediated by fibers that pass back into area 4. In the following two experiments the spinal terminal distribution of these fibers has been determined.

EXPERIMENT 3 (pyramidal *bouton* series, no. 6).—The right cerebral cortex of a rhesus monkey was exposed (March 29, 1934). The anterior boundary of

Fig. 3 (experiment 2; Macaca mulatta).—Tracing of the right cerebral hemisphere. The stippled part indicates the lesion in the premotor area.

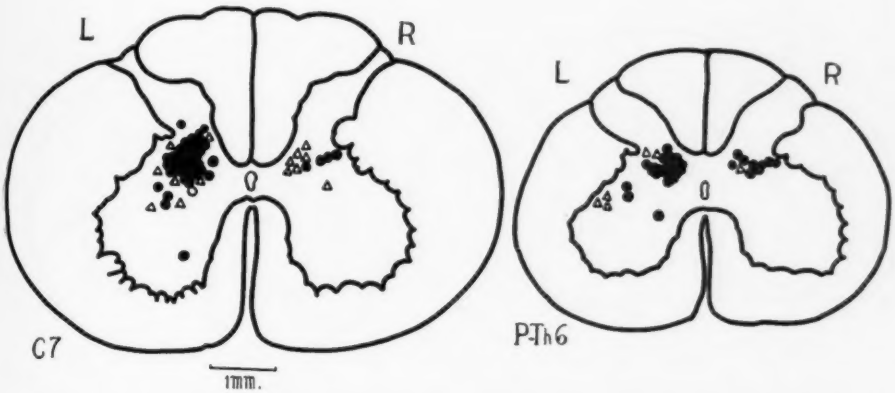


Fig. 4 (experiment 2).—Sections of the spinal cord at the seventh cervical and sixth postthoracic segments, showing the distribution of *bouton* degeneration in the spinal gray matter of a macaque killed four days after ablation of the right premotor area. The black circles and triangles have the same significance as in figure 2. (The diagram was drawn with a projector.)

the motor area was located by monopolar faradic stimulation, and a crescent-shaped incision completely separating areas 4 and 6 was made on the cortex to a depth of about 3 mm. The site of this incision is shown in figure 5.

It was impossible to elicit involuntary grasping at any time in the postoperative period, but a slight weakness of the left upper extremity was present.

On April 2, 1934, bipolar faradic stimulation elicited vigorous responses from the motor areas in the contralateral lower limbs, hand, arm and face. With stronger stimuli isolated movements of the contralateral upper and lower limbs were obtained from the left premotor area. The right premotor area was inexcitable to these stimuli and responded only after great increase of current strength by mass movements of the opposite side. Anesthesia was then deepened, and the animal was killed in the usual manner.

Histologic Observations of the Localization of the Lesion: Examination of serial sections through the right precentral gyrus demonstrated that the area of Betz cells had not been encroached on by the slit.

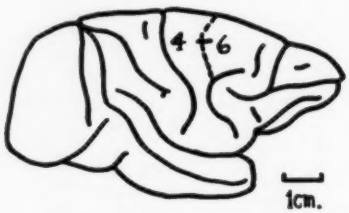


Fig. 5 (experiment 3; Macaca mulatta).—Tracing of the right cerebral hemisphere. The superficial cortical incision between the motor and premotor areas is denoted by the broken line.

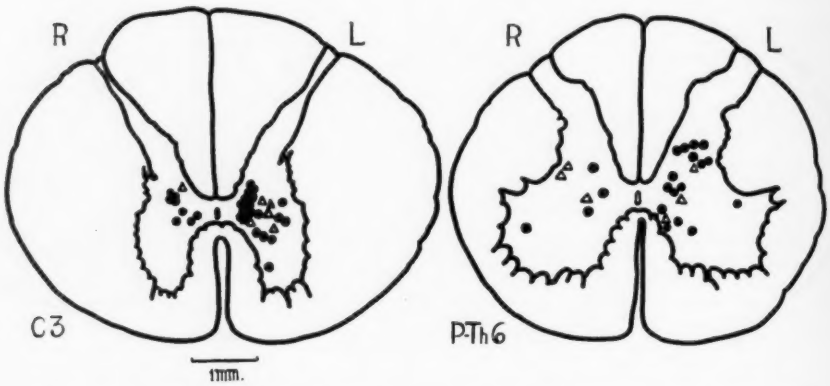


Fig. 6 (experiment 3).—Sections from the third cervical and sixth postthoracic segments of the cord of a macaque killed three days after a superficial incision between the right motor and premotor areas. The black circles and triangles have the same significance as in figure 2. (The diagram was drawn with a projector.)

Examination of *Bouton* Degeneration in the Cord (fig. 6): Nearly all the degeneration in the gray matter of this cord was on the contralateral side, where the degenerated terminals occurred chiefly on cells in the midregion and to a lesser extent in the ventral horn. On the ipsilateral side the number of degenerated terminals was less than one-fourth that on the opposite side, and the total amount

of degeneration in these sections was definitely less than that in experiments 1 and 2.

EXPERIMENT 4 (pyramidal *bouton* series, no. 9).—On Jan. 24, 1934, the left cerebral hemisphere of a rhesus monkey was exposed, revealing complete absence of the falx cerebri at every point along the exposed part of the hemisphere. A subsequent examination showed that the medial surfaces of the two hemispheres were separated only by the pia-arachnoid. The chief markings of the left hemisphere were made on a cellophane tracing (fig. 7), and the cortex was incised to a depth of from 4 to 5 mm. along a line parallel to the central sulcus and passing

Fig 7 (experiment 4; Macaca mulatta).—Tracing of the left cerebral hemisphere. The incision between the motor and premotor areas is indicated by the broken line.

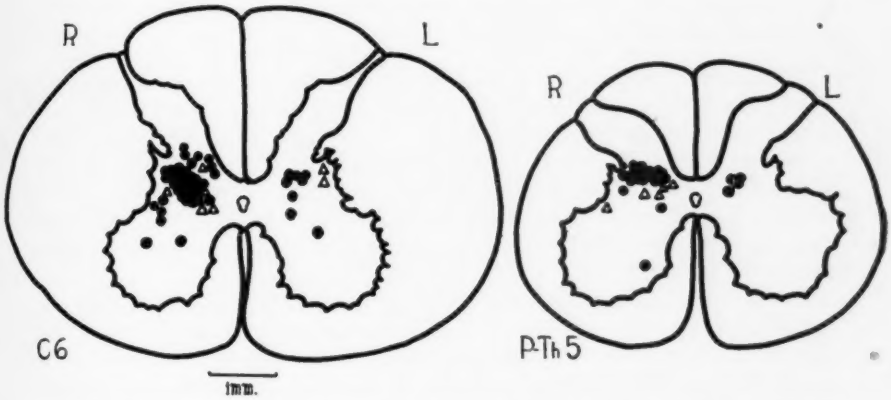


Fig. 8 (experiment 4).—Sections of the cord at the levels of the sixth cervical and fifth postthoracic segments, showing the distribution of *bouton* degeneration in the spinal gray matter. Three days before the animal was killed the cortex had been incised to a depth of from 4 to 5 mm. between the left motor and premotor areas. (The diagram was drawn with a projector.)

through the posterior end of the superior precentral sulcus. The incision was carried from the midline to a point a few millimeters beyond the inferior end of the arcuate sulcus.

During the postoperative period the animal showed some weakness of both right extremities, but there was no forced grasping.

On Jan. 27, 1934, both motor and premotor areas were exposed for stimulation. On monopolar faradization well marked characteristic responses were obtained from the right and left motor areas and the right premotor area. No sustained, isolated responses were obtained from the left premotor area, but with very strong stimuli generalized rhythmic movements of both contralateral extremities could be evoked. More profound anesthesia was then induced, and the monkey was killed by the injection of 500 cc. of 10 per cent chloral hydrate. Cajal preparations were made of sections across the region of the cortical lesion and of the cord.

Histologic Observations: The cortical incision lay slightly anterior to the area gigantopyramidalis, and no Betz cells showed evidence of involvement. Examination of sections of the spinal cord showed that degeneration occurred chiefly in the contralateral gray matter and that it was noticeably restricted to the midregion. In the cervical segments degenerated *boutons* were found predominantly around cell bodies lying in a band across the midregion with scattered endings in the dorsal part of the ventral horn and the base of the dorsal horn (fig. 8). In the postthoracic enlargement, the area of degeneration was more dorsally situated and involved cells lying in a band across the base of the dorsal horn of the contralateral gray matter. At all levels of the cord there was only a scant ipsilateral degeneration.

It is believed, therefore, that a direct corticospinal fiber system originating in area 6 and running superficially into area 4 exists. These fibers may give off collaterals which terminate about cells of the motor area; it is possible also that short axons arising in area 6 proceed superficially to end in the motor area.

Extirpation of Premotor Area After Destruction and Degeneration of Its Fiber Connections with Other Cortical Regions of the Frontal Lobe.—EXPERIMENT 5 (pyramidal *bouton* series, no. 12; premotor area, no. 38).—The left cerebral cortex of a rhesus monkey was exposed (Feb. 22, 1934). The anterior limit of the excitable motor cortex was determined by monopolar faradic stimulation and indicated on a cellophane tracing of the cortex (fig. 9). An incision about 5 mm. deep was made along this boundary from the midline to a point opposite the lower part of the face area.

Three hours after the operation the animal recovered from the anesthetic and showed a flaccid motor paralysis in the right upper extremity and weakness without definite paralysis in the right lower extremity. This weakness disappeared on the second day, and during the remainder of the postoperative period the animal showed no motor deficit. No forced grasping could be evoked at any time.

On March 12, 1934, the left cerebral cortex was reexposed, and all the premotor area anterior to the cortical slit was extirpated in one block.

On the second and third days after this second operation moderately well-marked forced grasping was elicited from the right upper extremity. The animal was killed on March 15, 1934.

Histologic Observations: On examination of the left motor area it was seen that the cortical slit lay at the anterior boundary of the area gigantopyramidalis. A few Betz cells were destroyed by the first operation, but as their terminal *boutons* had completely disintegrated they would not complicate the degeneration from the premotor area.

There was well marked bilateral degeneration in the cord almost entirely restricted to the base of the dorsal horn and the midregion of the gray matter. The amount of degeneration on the contralateral side was about twice that on the ipsilateral side, and the total number of degenerated *boutons* was less than after superficial slits between areas 4 and 6 or after simple extirpations of the premotor area (fig. 10).

Corticospinal projection systems which do not depend on the integrity of superficial connections between areas 4 and 6 are thus seen to originate in the premotor area. That they are not destroyed by the extirpation

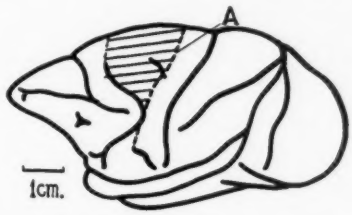


Fig. 9 (experiment 5; Macaca Mulatta).—Tracing of the left cerebral hemisphere. The broken line *A* indicates the cortical incision between the motor and premotor cortex; the cross-hatched area, the premotor cortex which was extirpated in the second operation.

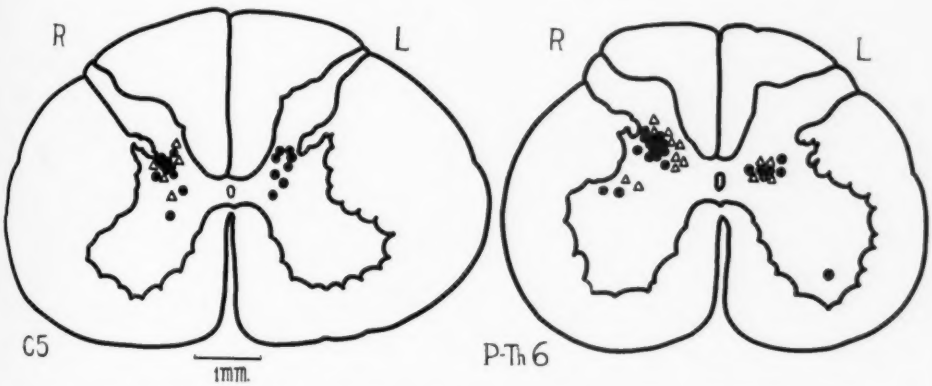


Fig. 10 (experiment 5; Macaca Mulatta).—Sections of the cord at the levels of the fifth cervical and postthoracic segments, showing the distribution of terminals of corticospinal fibers arising in the left premotor area. The black circles and the triangles have the same significance as in figure 2. (The diagram was drawn with a projector.)

of both the motor and the frontal area is shown in the following experiment.

EXPERIMENT 6 (pyramidal *boutons* series, no. 11; premotor area series, no. 13).—In a young baboon the left and right motor areas and the left and right frontal

areas were removed seriatim in four operations, so that only the premotor areas remained (fig. 11). Sixty-nine days after the last of these extirpations (Feb. 7, 1934) the intact right premotor area was removed (fig. 11 *B*).

During the three day postoperative period forced grasping was present in the left upper extremity together with a striking spasticity of both left extremities. On Feb. 10, 1934, the animal was killed.

Histologic Observations: Examination of serial sections (stained by the Nissl technic) of the block of cortical tissue removed from the right precentral

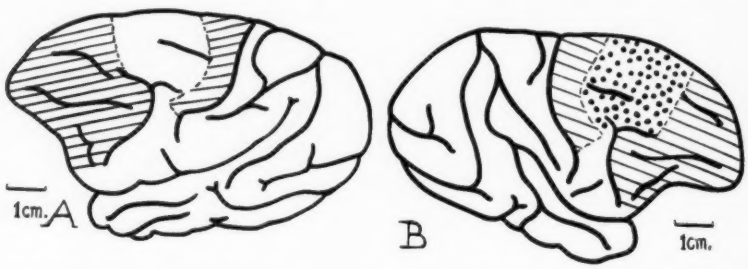


Fig. 11 (experiment 6; Baboon).—Tracings of the left (*A*) and of the right (*B*) cerebral hemisphere. The cross-hatched areas indicate the left and right motor areas and the left and right frontal areas, which were extirpated in four successive operations. In *A* the right premotor area, which was removed in the last operation, is indicated by small black dots.

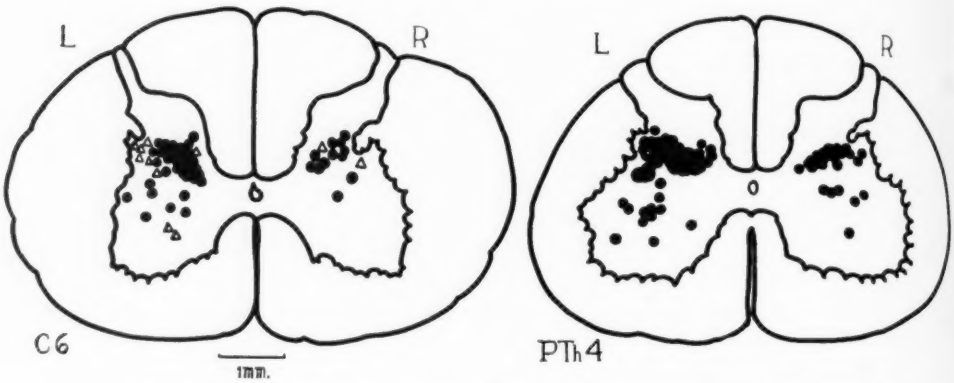


Fig. 12 (experiment 6).—Sections of the spinal cord of a baboon taken at the levels of the sixth cervical and fourth postthoracic segments, showing the distribution of *bouton* degeneration in the gray matter. These drawings indicate the terminal distribution of corticospinal fibers from the premotor cortex which are not damaged by the destruction of the motor and premotor areas of both sides. The black circles and triangles have the same significance as in figure 2. (The diagram was drawn with the aid of a projector.)

gyrus showed that the entire Betz cell area had been extirpated in the earlier operation together with a small amount of the premotor cortical tissue lying opposite the lower part of the brachial area and the upper part of the representation

of the face. Therefore, any *bouton* degeneration resulting from the final operation did not arise from the section of axons of the Betz cell area.

As in the preceding experiment the degeneration in the cord was bilateral and was largely limited to the base of the dorsal horn. However, many degenerated terminals were also scattered throughout the ventral horn, chiefly on the smaller cell bodies. The ratio of degeneration on the two sides of the cord was about the same as in the preceding experiment (fig. 12).

COMMENT

The evidence presented permits the conclusion that in the monkey direct corticospinal projection fibers originate in the premotor area as well as in the so-called motor cortex. One group of these fibers passes superficially into the motor area and is projected into the cord in the pyramidal tracts, ending for the most part in the contralateral gray matter at the base of the dorsal horn. The premotor cortex also gives rise to long projection fibers which are not damaged by superficial cortical slits between the motor and premotor areas or ablation of both motor and frontal areas. These fibers are shown to end bilaterally at all levels of the cord, chiefly in the midregion of the gray matter.

Physiologic evidence [1] suggests strongly that, in addition to the long corticospinal fibers discussed in this paper, the premotor cortex gives origin as well to short projection systems ending in subcortical supraspinal centers. The course and terminations of these fibers are at present being investigated.

SUMMARY

1. The method of *bouton* degeneration has been employed to study the endings of fibers originating in the premotor cortex (area 6 of Brodmann).

2. These investigations have demonstrated that this area gives rise to fiber tracts which pass without interruption into the cord, where they form synaptic connections with spinal neurons.

3. Many of these corticospinal fibers pass superficially from the premotor into the motor cortex (area 4 of Brodmann), whence they are projected into the cord, ending for the most part around cells at the base of the dorsal horn of the contralateral gray matter. A smaller proportion of these fibers ends in the corresponding region of the ipsilateral side. A few scattered endings occur around cells of the dorsal part of the ventral horn of both sides.

4. Another group of projection fibers, independent of the motor area, terminates on neurons restricted largely to the midregion of the gray matter of both sides of the cord.

CORTICOSPINAL FIBERS ARISING IN THE PREMOTOR AREA OF THE MONKEY

AS DEMONSTRATED BY THE MARCHI METHOD

MARGARET A. KENNARD, M.D.
NEW HAVEN, CONN.

In a recent attempt to trace the anatomic connections of the frontal lobe of the monkey, degenerations have consistently been found in the spinal cord following ablations restricted to the premotor area. As the existence of nonpyramidal corticospinal fibers has not hitherto been recognized, a systematic examination of their course, as well as of their cells of origin, has been undertaken, and this article records the results of this study.

Histologically, the premotor and motor areas of the cortex, which are designated as areas 6 and 4, respectively, in Brodmann's architectonic map [1] (fig. 1), are identical except for the absence in the premotor area of the giant pyramidal cells of Betz. Ablation experiments [2] had suggested that the pyramidal tracts originated solely from the motor area, and Holmes and May,[1b] who studied retrograde cellular degeneration in the cortex after lateral semisection of the cord, concluded that the Betz cells give rise only to corticospinal fibers and, conversely, that corticospinal fibers originate only in the Betz cells.

PREVIOUS OBSERVATIONS

Uncrossed Corticospinal Tracts.—Though corticospinal fibers were at first regarded as crossing completely at the decussation, it was shown early that some

---

From the Laboratory of Physiology, Yale University School of Medicine.

The material included in this article formed a part of a communication by J. F. Fulton, E. C. Hoff and Margaret A. Kennard read at the Sixtieth Annual Meeting of the American Neurological Association at Atlantic City, N. J., June 4, 1934, under the title, "The Distribution of Corticospinal Fibers from the Premotor Area as Shown by the *Boutons Terminaux* and Marchi Techniques."

1. (*a*) Brodmann, K.: Vergleichende Lokalisationslehre der Grosshirnrinde in ihren Prinzipien dargestellt auf Grund des Zellenbaues, Leipzig, Johann Ambrosius Barth, 1925. (*b*) Holmes, G., and May, W. P.: On the Exact Origin of the Pyramidal Tract in Man and Other Mammals, Brain **32**:1 (May) 1909.

2. (*a*) Hadden, W. B., and Sherrington, C. S.: On a Case of Bilateral Degeneration in the Spinal Cord Fifty-Two Days After Hemorrhage in One Cerebral Hemisphere, Brain **8**:502 (Jan.) 1886. (*b*) Sherrington, C. S.: Note on Experimental Degeneration of the Pyramidal Tract, Lancet **1**:265 (Feb. 3) 1894. (*c*) Mellus, E. L.: Preliminary Note on Bilateral Degeneration in the Spinal Cord of Monkeys (Macacus Sinicus) Following Unilateral Lesions of the Cortex Cerebri, Proc. Roy. Soc. London **55**:208 (March) 1894.

fibers descended in the ipsilateral ventral and lateral parts of the cord. Hadden and Sherrington,[2a] in 1886, described a human case of bilateral degeneration of the cord after hemorrhage in one cerebral hemisphere. In 1894 Sherrington [2b] and Mellus [2c] each found, after unilateral ablation of the motor cortex in the monkey, that descending degenerations were present on both sides of the cord, and in 1896 Dejerine and Thomas [3] reported seven human cases in which lesions in one hemisphere were followed by degeneration in the ipsilateral ventral and lateral columns as well as in the contralateral descending tract. Spiller, in 1898,[4] corroborated these observations in a case of congenital absence of the left pyramid in which the patient showed some voluntary motor power in the right leg, although the right arm was completely paralyzed. The corticospinal pathways for ipsilateral movement have been assumed to be these ipsilateral pyramidal tracts, both the ventral and the lateral pathway originating in the Betz cells of the motor area.

More recently certain motor phenomena have come to be assigned to areas other than the motor area of the cortex. Adie and Critchley [5] first pointed out that forced grasping develops in man when the region just rostral to the motor area is injured. Richter and Hines [6] proved that in monkeys forced grasping is a purely cortical phenomenon which follows lesions sharply restricted to the premotor area, and Fulton, Jacobsen and Kennard [7] confirmed this observation and found that other reflex changes are regularly associated with premotor lesions. Similar changes have recently been found in a human case.[8]

Motor effects, have been produced, moreover, by faradic stimulation of the premotor area after complete degeneration of the pyramidal tracts (Bucy [9]). Specific responses to faradic stimulation of this area had previously been described by Campbell,[10] by Holmes and May [1b] and by C. and O. Vogt,[11] but these reactions had not been adequately

3. Dejerine, J., and Thomas, A.: Sur les fibres pyramidales homolatérales et sur la terminaison inférieure du faisceau pyramidal, Arch. de physiol. norm. et path. **8**:277, 1896.

4. Spiller, W. G.: Case Report, Philadelphia M. J. **1**:465 (March 12) 1898.

5. Adie, W. J., and Critchley, M.: Forced Grasping and Groping, Brain **50**:142 (June) 1927.

6. Richter, C. P., and Hines, M.: Experimental Production of the Grasp Reflex in Adult Monkeys by Lesions of the Frontal Lobes, Am. J. Physiol. **101**:87 (June) 1932.

7. Fulton, J. F.; Jacobsen, C. F., and Kennard, Margaret A.: A Note Concerning the Relation of the Frontal Lobes to Posture and Forced Grasping in Monkeys, Brain **55**:524 (Dec.) 1932.

8. Kennard, Margaret A.; Viets, H. R., and Fulton, J. F.: The Syndrome of the Premotor Cortex in Man; Impairment of Skilled Motor Cortex in Man; Impairment of Skilled Movements, Forced Grasping, Spasticity, and Vasomotor Disturbance, Brain **57**:69 (May) 1934.

9. Bucy, P. C., and Fulton, J. F.: Ipsilateral Representation in the Motor and Premotor Cortex of Monkeys, Brain **56**:318 (Sept.) 1933.

10. Campbell, A. W.: Histological Studies on the Localisation of Cerebral Function, London, Cambridge University Press, 1905.

11. Vogt, Cécile, and Vogt, O.: Allgemeinere Ergebnisse unserer Hirnforschung, J. f. Psychol. u. Neurol. **25**:277, 1919.

separated from those induced by stimulation of the motor area. It has thus become increasingly evident that the premotor area is the source of a well defined motor projection system.

What, then, is the course of defferent impulses originating in this area? The prevailing idea is that neurons originating in regions of the frontal lobe other than the motor area end in other cortical areas, or at way stations in the brain stem. This is the case with many fibers of the premotor area, some of which cross in the corpus callosum to the premotor area of the opposite hemisphere [12] and some of which sweep backward into the motor area of the same side.[9]

That corticospinal fibers also arise from the premotor area in the monkey is shown by the following series of experiments. These fibers were present in all the preparations examined and were found in both the contralateral and the ipsilateral columns of the cord.

PROCEDURES

Observations on degeneration due to lesions of the premotor area have been made incidentally in connection with the study of other problems on forty monkeys and baboons during the past three years. This report, however, is based on observations on nine animals which were used solely for the investigation of this special problem. They were in good condition and had no motor abnormality before operation. Seven belonged to the species Macaca mulatta (rhesus) and two to the species Cercopithecus aethiops sabaeus (green). All were immature and weighed between 2,000 and 4,000 Gm. Our incidental observations had indicated that bilateral degeneration occurred consistently in the cord after lesions of the premotor area, and because of this the present study was undertaken.

Operation was performed under sodium amytal anesthesia with aseptic technic.[13] A flap of bone was reflected, and the normal markings of the cortex were traced on cellophane. The boundaries of the motor area were then defined by monopolar faradic stimulation, and an extirpation was carried out either anterior or posterior to the line at which faradic stimulation ceased to give discrete motor responses in the contralateral extremities. The point at which excitability by faradic stimulation changes, at the anterior limit of the motor area of the cortex, has been found by Bucy [14] to correspond closely to the region in which the large pyramidal cells of Betz disappear from the fifth layer of the cortex. Extirpations from the motor area included the areas of representation for the leg, the body and the arm, but the area for the face was always left intact. The premotor area extirpated extended from the motor area posteriorly to the mesial fissure on the midsurface of the hemisphere and to the arcuate sulcus inferiorly. The anterior border extended from the anterior corner of the arcuate sulcus superiorly to the midline (fig. 1).

---

12. Kennard, Margaret A., and Watts, J. W.: The Effect of Section of the Corpus Callosum on the Motor Performance of Monkeys, J. Nerv. & Ment. Dis. **79**:159 (Feb.) 1934.

13. Fulton, J. F., and Keller, A. D.: The Sign of Babinski: A Study of the Evolution of Cortical Dominance in Primates, Springfield, Ill., Charles C. Thomas, Publisher, 1932.

14. Bucy, P. C.: Electrical Excitability and Cyto-Architecture of the Premotor Cortex in Monkeys, Arch. Neurol. & Psychiat. **30**:1205 (Dec.) 1933.

Eight of the animals were killed from eighteen to twenty-one days after the cortical extirpation. The ninth (experiment 1), because it was being observed in another series of experiments, was kept forty-one days before being killed, but it showed marked degeneration along the pyramidal tracts.

The animals were killed under anesthesia, and the brain and spinal cord were placed in Müller's solution [15] and eventually sectioned and stained by the Marchi technic under the supervision of Dr. H. M. Zimmerman of the Department of Pathology. Portions of the cortex, both the part extirpated at operation and the surrounding tissue removed at autopsy, were placed in alcohol and stained by the Nissl method. Usually three or four sections were made through the block which had been extirpated, but occasionally serial sections of the entire block were cut.

For the Marchi material, sections were cut through the corpus callosum, internal capsule (left and right), pons, medulla and decussation of the pyramids and through the cord at high and low cervical, midthoracic and lumbar levels.

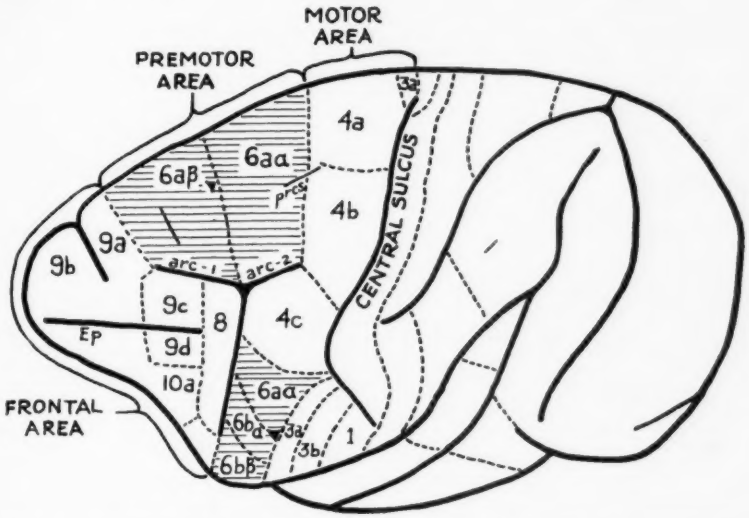


Fig. 1.—Diagram of the left hemisphere of the brain of a Macacus rhesus monkey, showing three areas of the frontal lobe and their anatomic divisions (after C. and O. Vogt [11]).

OBSERVATIONS

The experiments may be divided into four groups as follows: (1) extirpations of the motor area, (2) extirpations of the premotor area, (3) extirpations of the motor plus the premotor area and (4) extirpations of the frontal lobe in regions other than the premotor and motor areas. The general results are indicated in the following illustrative protocols.

Extirpations of the Motor Area.—Experiment 1 (area 6, series no. 3).—The left motor area was removed from a healthy rhesus monkey on Jan. 12, 1933.

15. Müller's solution consists of a solution of 2.5 Gm. of potassium dichromate and 1 Gm. of sodium sulphate for each one hundred cubic centimeters of water.

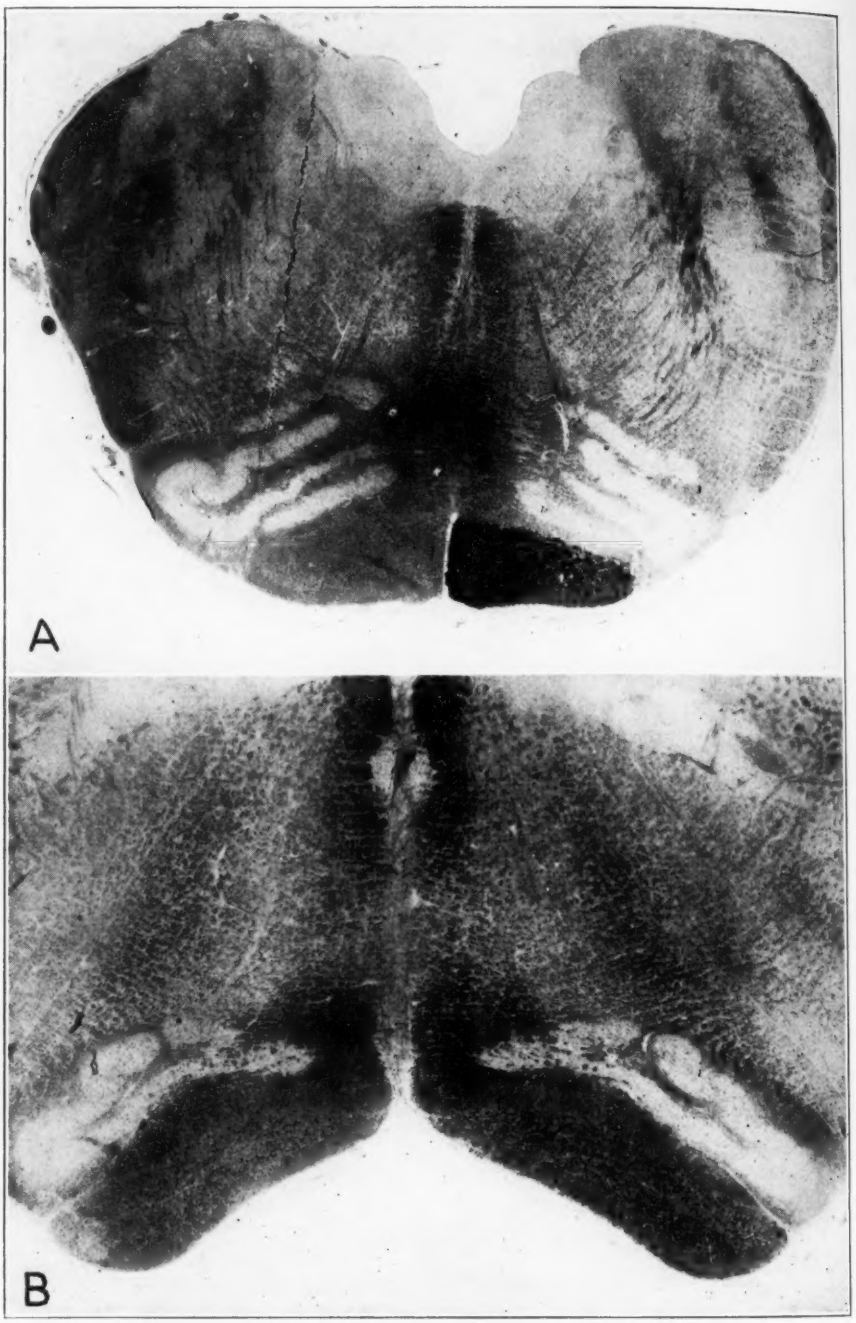


Fig. 2.—Marchi degeneration in the left pyramidal tracts in two monkeys: *A*, after extirpation of the motor area (experiment 1); *B*, after extirpation of the premotor area (experiment 4).

After operation the animal had a characteristic flaccid hemiparesis on the right side, with slow recovery of function. It was killed on Feb. 23, 1933.

Examination of the block of tissue extirpated at operation showed the large pyramidal cells of Betz extending over the posterior two thirds of the section. About 2 mm. of the anterior portion contained no pyramidal cells and must therefore have been from the premotor area.

Marchi sections from the cord and the medulla showed grossly degenerated tracts which passed via the left internal capsule and pyramid into the spinal cord. In the cord, from the second cervical to the second sacral level, this degeneration occurred in three different areas. The right dorsolateral column contained heavy degeneration, the left dorsolateral column showed slight degeneration scattered throughout the entire area, and the left ventral column also showed distinct degeneration.

EXPERIMENT 2 (premotor area, series no. 40).—The left motor area was extirpated from a rhesus monkey on April 20, 1934, without involvement of area 6. The animal exhibited a characteristic flaccid paresis on the right side; power returned slowly, and it was killed on May 8, 1934.

Nissl sections of the extirpated area revealed Betz cells throughout the block, and there was no evidence of encroachment on the premotor area. There was Marchi degeneration at the genu of the internal capsule and in the pons on the left side. Below the decussation the right dorsolateral column contained many degenerated fibers; the corresponding area on the left showed a small number of fibers evenly scattered throughout the tract. There were also a few degenerated fibers in the left ventral column.

Extirpation of the motor area in these instances, therefore, led to degeneration of descending fiber systems, the course of which could be definitely traced through the central nervous system as far caudally as the second sacral level. The fibers passed from the motor area of the cortex to the internal capsule of the same side, where they ran just anterior to the genu, and descended in the pyramidal tract to the decussation. There the majority of the fibers crossed to the contralateral column of the cord. A certain number, however, passed downward in the lateral ipsilateral column, and others, in the ventral ipsilateral column.

Extirpations of the Premotor Area.—EXPERIMENT 3 (premotor area, series no. 26).—On Dec. 4, 1933, the left premotor area was extirpated from a healthy immature male rhesus monkey. The animal showed spastic hemiparesis on the right side accompanied by forced grasping during the first postoperative week. Voluntary power returned slowly in both right extremities. Forced grasping disappeared by the end of the second week, and motor performance appeared normal at the time when the animal was killed (Dec. 27, 1933).

On histologic examination no Betz cells were seen in the block extirpated at operation. Marchi degeneration was present in the left internal capsule at the genu, but there was none in the right internal capsule. Degeneration could be traced through the medulla in the left pyramidal tract and at the decussation; by far the greater number of the fibers passed over to the right dorsolateral column of the cord (fig. 4*B*). The total degeneration was less than that seen in motor area preparations, but the fibers were scattered in even distribution over the entire area occupied by the pyramidal tract. On the ipsilateral side of the cord also degeneration was present in the dorsolateral column, but less extensively

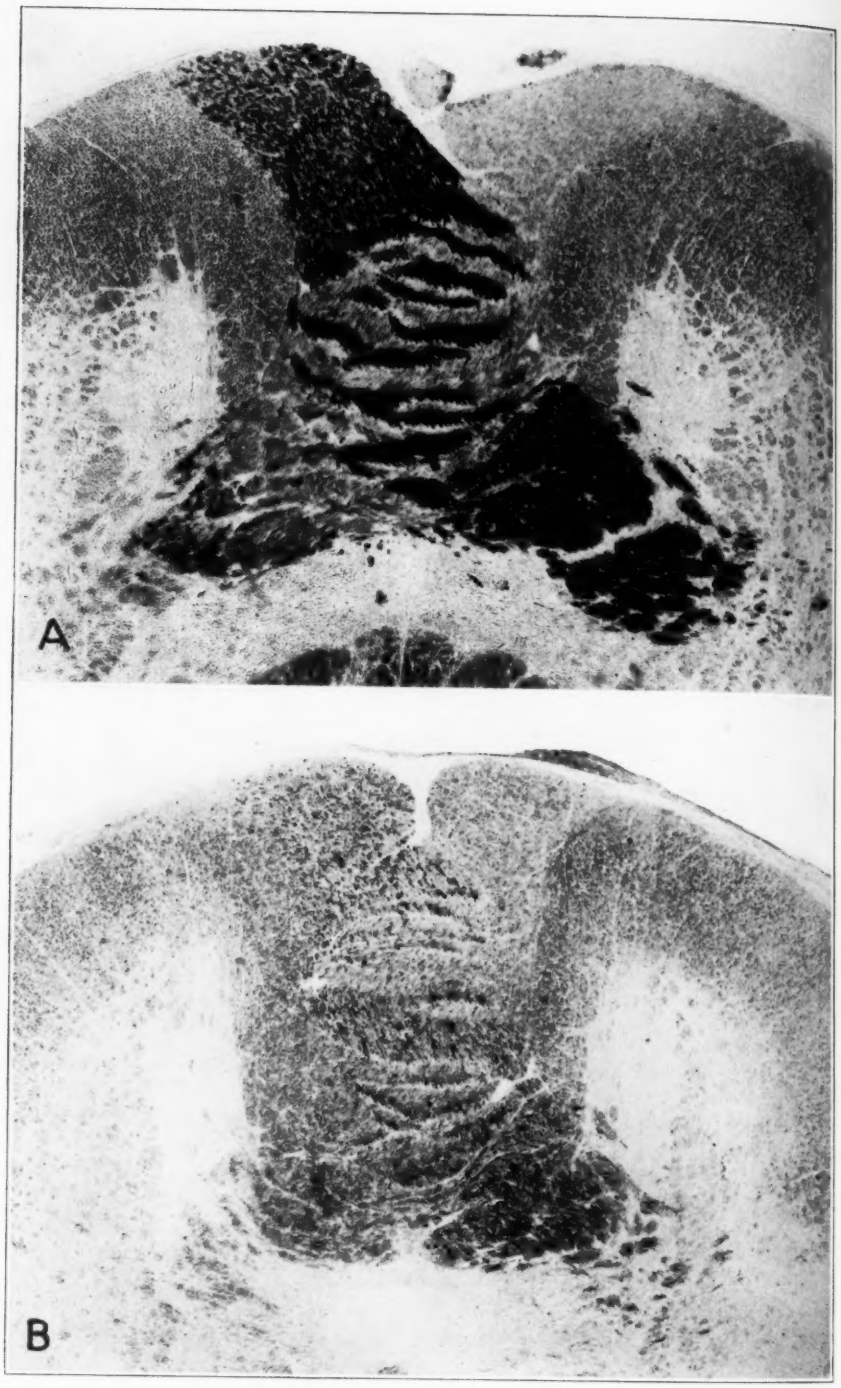


Fig. 3.—Marchi degeneration at the decussation of the pyramids: *A*, after extirpation of the motor plus the premotor area (experiment 7); *B*, after extirpation of the premotor area (experiment 4). Note the ipsilateral fibers in both instances.

than on the contralateral side. The proportion of ipsilateral to contralateral fibers was, however, much greater in this premotor preparation than after lesions of the motor area. No degeneration was present in the ventral column of either side.

EXPERIMENT 4 (premotor area, series no. 32).—Under sodium amytal anesthesia an extirpation of the left premotor area was carried out in a normal rhesus monkey on Jan. 23, 1934. Following the operation the right extremities showed a characteristic transient spastic paresis associated with forced grasping. A residual weakness and awkwardness of these limbs were present when the animal was killed, Feb. 12, 1934.

Sections through the extirpated premotor area showed five large pyramidal cells in a group on one slide. Otherwise the cortical gray matter showed only the five cortical layers characteristic of the premotor area.

There was marked fine Marchi degeneration in the middle third of the corpus callosum. Degeneration in the pyramidal tracts above the decussation was entirely unilateral and confined to the left pyramid. Below, the contralateral tract contained numerous evenly distributed degenerated fibers, and on the ipsilateral side as well there was a well defined but much more slight degeneration.

EXPERIMENT 5 (premotor area, series no. 21).—A normal young male green monkey was operated on on Oct. 10, 1933. Only the anterior part of the premotor area was extirpated, i. e., area 6a β. After operation the animal showed no gross deficit. Forced grasping was present for about ten days but was difficult to determine because of the superimposed voluntary grasp. However, it was very definite and was affected by changes in the position of the animal in space.

On November 1, the animal was killed under deep anesthesia. Serial sections through the area originally extirpated showed occasional islands of large pyramidal cells scattered in the fifth layer. These cells appeared to be as large as the motor Betz cells and were in groups of 5 or 6 together; not more than 30 cells of this type were seen in all. An examination of the tissue posterior to the site of extirpation revealed a definite line of demarcation from 3 to 4 mm. behind the anterior cut surface where the Betz cells stopped. This was considered in this preparation, as in all others, as the anterior boundary of the motor area.

Marchi degeneration was seen in the left internal capsule at the genu, but there was none in the right internal capsule. It appeared in the left pyramid above the decussation and was present bilaterally below that region. It was definite but very slight on the ipsilateral side of the cord, and on the contralateral side it was plentiful and spread throughout the pyramidal tract, although the number of fibers was much less than that seen after extirpation of the entire premotor area.

EXPERIMENT 6 (premotor area, series no. 38).—On Feb. 22, 1934, the left cortex of an immature female rhesus monkey was exposed under light anesthesia. The anterior limits of the excitable motor area were defined by monopolar faradic stimulation, and a slit was then made through the gray matter of the cortex, along a line parallel to the anterior border of the motor area. This was done in order to observe what degeneration might take place in the cord from fibers originating in the premotor area but passing to the lower levels by way of the motor area. Care was taken to make the incision in the excitable region since it was desired to injure only the fibers which sweep back from the premotor area and to do no damage to the cells in area 6 itself. On the day after operation the animal showed a moderate degree of paresis of the right extremities; the paresis was greater in the arm. It was of the flaccid type, and there was no forced grasping. Forty-eight hours after operation all traces of motor deficit had disappeared.

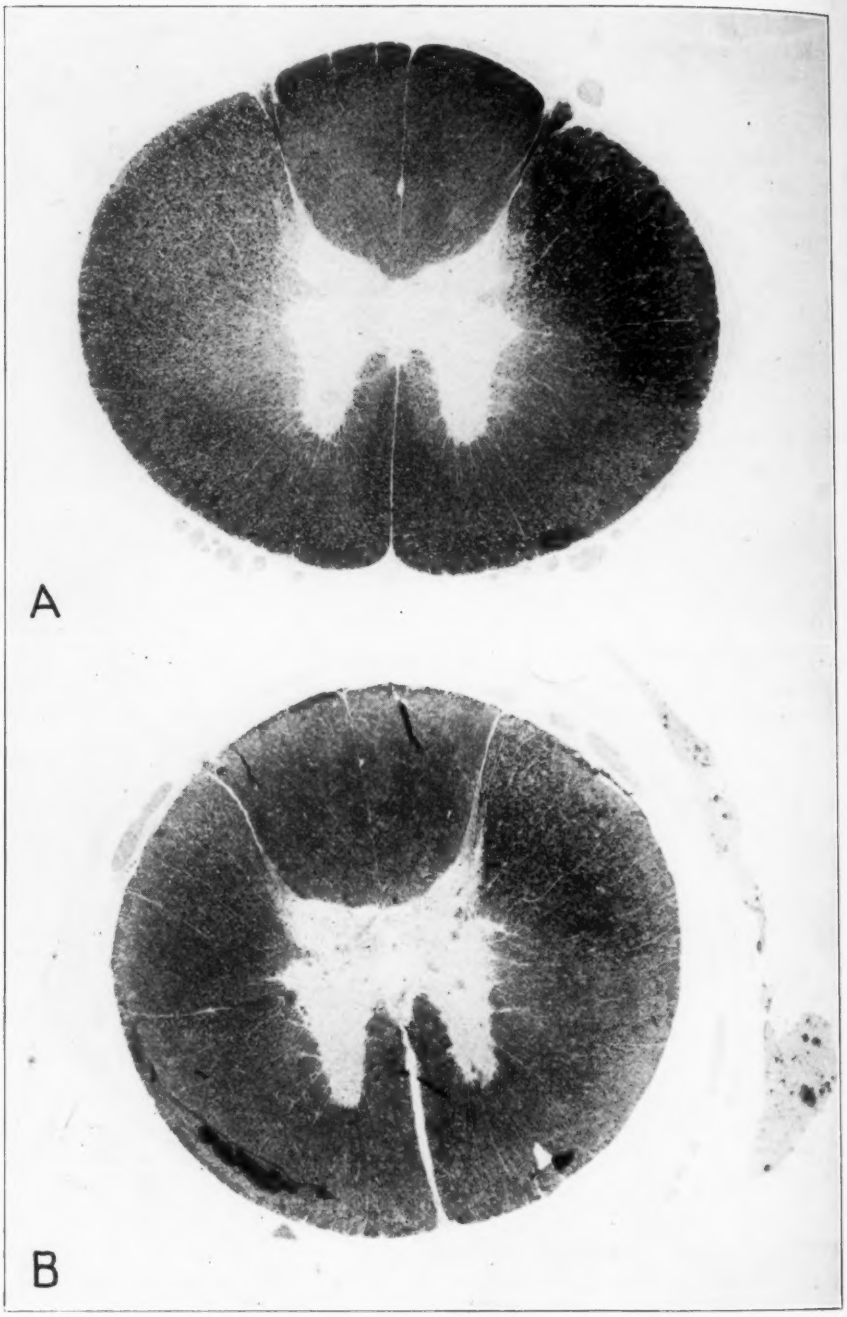


Fig. 4.—Bilateral Marchi degeneration in the lumbar portion of the cord: *A*, after extirpation of the motor area (experiment 1); *B*, after extirpation of the premotor area (experiment 3).

Histologic examination after autopsy (March 15, 1934) revealed that the anterior limit of the Betz cells was just rostral to the line of scar tissue made by the original operation. The section had therefore been made within the limits of area 4.

There was definite degeneration in both dorsolateral columns of the cord, but on neither side was it as great as that seen when the entire premotor area was extirpated. On the ipsilateral side the degenerated fibers were very few and widely scattered; on the contralateral side there was much more degeneration, but again not as much as with complete extirpation of area 6. The number of degenerated fibers on each side was, however, greater than that seen in experiment 4, in which the anterior part of area 6 was removed.

Extirpations of the premotor area in which there is no involvement of the large pyramidal cells of Betz result in degeneration of descending cortical projection fibers which pass downward along what are commonly called the pyramidal tracts to the lower lumbar levels of the cord. Such degeneration is not so great as that produced by lesions of the motor area alone, especially in the contralateral column of the cord. In the ipsilateral column also it is less than after lesions of the motor area, but the number of ipsilateral in proportion to contralateral degenerated fibers is relatively much greater after extirpations of the premotor than after extirpation of the motor area. This degeneration in the cord is due in part to fibers which pass from the premotor area to lower levels via the motor area, since a slit cut between these areas produces characteristic degeneration. Some fibers, however, must pass more directly downward from area 6, since degeneration produced by the slit is not so great as that following complete extirpation of the premotor area. Removal of the anterior half of the premotor area results in slight but definite bilateral degeneration in the cord. No degeneration was seen in the ventral ipsilateral column following extirpation of the premotor area.

Extirpations of the Motor Plus the Premotor Area.—EXPERIMENT 7 (premotor area, series no. 19).—The entire motor and premotor areas were removed at one operation from the left cortex of a young green monkey (Oct. 7, 1933). Spastic paresis appeared in the right arm and leg. Voluntary power returned slowly during the first week. Forced grasping was marked but disappeared five days after operation. The spasticity and awkwardness in motor performance persisted until the animal was killed (Oct. 27, 1933).

The degeneration in the pyramidal tracts followed the usual course and distribution. It was, however, extremely heavy, particularly in the contralateral column of the cord. Ipsilateral degeneration in the lateral column was also slightly greater than that seen in pure extirpations of the motor area.

Simultaneous extirpation of the two areas, motor and premotor, is followed by heavy degeneration in descending fibers which pass through the internal capsule via pyramidal tracts to the decussation. A very great number of the fibers cross at that site, but some remain on the ipsilateral side of the cord in the dorsolateral and ventral columns.

Degeneration after this type of extirpation is greater than after removal of area 6 or area 4 alone, especially in the contralateral dorsolateral column of the cord.

Extirpations from Regions of the Frontal Lobe Other than the Premotor and Motor Areas.—EXPERIMENT 8 (premotor area, series no. 31).—The frontal area comprising all the tissue in the frontal lobe rostral to the motor and premotor areas (fig. 1) was extirpated from a Macacus rhesus monkey (Jan. 3, 1934). As is usual with preparations of this type there was no motor or postural change. The animal was killed twenty-one days later. Again, as is usual after frontal extirpations, there was no Marchi degeneration in the spinal cord in either pyramidal area.

EXPERIMENT 9 (corpus callosum series, no. 13).—The corpus callosum was completely sectioned (Jan. 9, 1934) in a Macacus rhesus monkey which showed no detectable motor deficit at any time after operation and was killed on Jan. 31, 1934.

Examination of the brain and cord showed bilateral degeneration of fibers running well into the cortex on either side from the cut corpus callosum. There were a few degenerated fibers throughout the right pyramidal tract, but as the degeneration was unilateral and the flap of bone had been made in the left tract, it was believed that trauma to cortical tissue at operation was responsible for these few degenerated fibers.

Ablation of tissue rostral to the premotor area in the frontal lobe and also section of the corpus callosum produced no significant degeneration at spinal levels in the central nervous system.

COMMENT

It is thus clear that in monkeys corticospinal degeneration occurs after lesions which do not injure the giant Betz cells in the motor area. Such degeneration is found after ablation of the premotor area but not from injury to the more rostrally situated frontal association areas. This nonpyramidal degeneration follows the anatomic course of the true pyramidal pathways. Some of the degenerating fibers sweep backward into the motor area and pass thence into the pyramidal tracts (experiment 6), but others pass directly downward to the internal capsule (experiment 5). Throughout the pyramidal pathways the premotor fibers are uniformly scattered among the pyramidal bundles. The majority of premotor fibers decussate, but a small proportion remain on the same side of the cord throughout their entire course. These are found in the dorsolateral column of the cord but not in the ventral column as are projection fibers from the motor area.

The total number of premotor fibers in the cord is far less than the number of true pyramidal fibers. From material stained by the Marchi method it is difficult to estimate the number of fibers involved in degeneration from the two areas, but quantitative differences are undoubtedly very great (fig. 4). In the internal capsule the chief degeneration occurs at the genu with both types of lesion. At the decussation (figs. 2 and 3)

the majority of fibers cross, and in the contralateral column of the cord degeneration from motor lesions is many times heavier than that from premotor lesions. After slitting the cortex between areas 6 and 4, or after removal of only a part of area 6, degeneration is less than when the entire premotor area is removed.

Ispilateral tracts arise in both the motor and the premotor region, but the motor area sends fibers to both the lateral and the ventral columns of the same side, while the fibers from the premotor area are found only in the lateral column. The ipsilateral representation from the premotor cortex is relatively much greater than that from the motor area, that is, the number of degenerated fibers in the ipsilateral lateral column appears nearly as great following lesions of the premotor area as after a lesion of approximately the same magnitude involving the motor area.

These observations have been confirmed in this laboratory by E. C. Hoff,[16] who, using the same operative technic, has studied degeneration of the *boutons terminaux* in the gray matter of the cord and who reported that both ipsilateral and contralateral degeneration occur after isolated lesions of the premotor as well as of the motor area.

Another point which merits consideration is the relation of the non-pyramidal corticospinal fibers to the isolated large pyramidal cells, which are sometimes found sporadically well anterior to the well defined anterior boundary of the motor area at which the Betz cells disappear. Groups of 5 or 6 such cells have frequently been found in Nissl preparations of the premotor area; they are large, triangular and comparable in size and structure to the smaller Betz cells of the motor area. Their number and distribution are inconstant, and in no animal has a sufficient number been disclosed to account for the degenerated spinal fibers. Thus, in complete serial sections in experiment 5 only 30 of these cells were seen, but the number of degenerated corticospinal fibers in one pyramidal area was many times greater. As estimated from the figures quoted by Tilney and Riley,[17] the number of Betz cells in the human motor area in one hemisphere is 25,000, and if these cells are the origin of the corticospinal fibers there must be not less than 25,000 fibers in the pyramidal tracts of the cord. The proportion of premotor fibers to motor fibers in the cord is certainly as much as 1:15 or 1:20. Thus, the number of aberrant large pyramidal cells found in the premotor

16. Hoff, E. C.: The Distribution of Spinal Terminals (*Boutons*) of the Pyramidal Tract, Determined by Experimental Degeneration, Proc. Roy. Soc. London, s.B **111**:226 (July) 1932. Hoff, E. C.: Corticospinal Fibers Arising in the Premotor Area of the Monkey: Distribution of Bouton Terminations, Arch. Neurol. & Psychiat., p. 687.

17. Tilney, F., and Riley, H. A.: Form and Functions of the Central Nervous System, New York, Paul B. Hoeber, Inc., 1923.

cortex cannot be sufficient to account for the number of premotor fibers, which is certainly more than 1,000. That the premotor fibers do not arise from the Betz cells in the true motor area is proved not only by the presence of degeneration following lesions of the rostral part of the premotor area but by the degree of degeneration found after the cortex is slit between the motor and the premotor area. Some source other than the gigantic pyramidal cells of Betz must, then, be the origin of nonpyramidal corticospinal fibers.

CONCLUSIONS

1. In monkeys nonpyramidal corticospinal fibers have been demonstrated by the presence of Marchi degeneration following extirpation of the premotor region of the cortex (area 6 of Brodmann).

2. The cells of origin of these fibers are in the premotor area, degeneration occurring when no injury has been done to the Betz cells of the motor area. The isolated groups of large pyramidal cells found occasionally in the fifth layer of the premotor cortex are too few to be considered.

3. Some corticospinal fibers pass directly downward from the gray matter of the cortex to the internal capsule of the same hemisphere, but others pass backward into the motor area before descending.

4. The number of degenerated corticospinal fibers present after lesions of the motor area is many times greater than the number present after lesions of the premotor area, especially in the contralateral column of the cord.

5. However, the ipsilateral representation of the premotor area is relatively greater than that of the motor area.

6. No corticospinal fibers are found originating rostral to the premotor area in the frontal association areas.

DISCUSSION

Dr. E. A. Spiegel, Philadelphia: The premotor area or area frontalis agranularis, of Brodmann, is of especial interest in many respects. It occupies in the human brain a large part of the precentral gyrus. Foerster has called attention to the fact that stimulation of this area gives rise to a special form of epileptiform convulsions. Furthermore, it is quite probable that the restitution of motor function after lesions of the Betz cell area partly has to do with the function of the premotor area. Foerster has expressed the opinion that the restitution of function after lesions of the motor area is due to extrapyramidal tracts originating in the premotor area. Many observers have expressed the opinion that the effects of stimulating this area are due to a spread of the current or irradiation on the motor area. The careful observations of Dr. Fulton and of his associates indicate that these opinions will have to be revised and that one must assume that there exist direct corticospinal fibers originating in area 6 of Brodmann. These facts

seem of particular importance in regard to the mechanism of the aforementioned forms of epileptiform convulsions and in regard to the compensatory mechanisms after lesions of the motor area.

Dr. Henry R. Viets, Boston: It has been my privilege to be associated with Dr. Fulton and Dr. Kennard in some of their work on the premotor area, and I think that the paper that has been read this afternoon is a logical part of the whole scheme that they have developed in working out the function of this area of the brain. Certainly great credit is to be given to Dr. Fulton and his co-workers for presenting information about the premotor area.

My interest in the premotor cortex arose because of observations made in Dr. Fulton's laboratory. We were able to apply the essence of these observations to certain cases; in one case, to localize a tumor, later successfully removed by surgical intervention. In studying the physiologic processes in that patient (*Brain* **57**:69 [March] 1934) it is interesting to note that fortunately, both the vocation and the avocation of the patient were of considerable help; he was a shoe salesman and one of the first difficulties that he had was in tying shoe-strings, a skilled movement that was lost before any other clinical symptom appeared. Also, the patient played the piano, and he found that his left hand, which was affected, had difficulty in carrying on the skilled movements required. He showed the whole "premotor syndrome" in chronological sequence before the tumor was diagnosed: inability to perform skilled movements, spasticity, forced grasping and vasomotor changes. Since the tumor has been removed the symptoms have disappeared in the reversed order, the vasomotor changes and spasticity disappearing along with the forced grasping, and now, after a year, the last deficit left is a slight loss of skilled movement noticed particularly in playing the piano. Otherwise he is quite free from signs of the disease. This report, therefore, shows the clinical application of the physiologic findings.

I wish to emphasize the importance of tracing the pathways, as Dr. Fulton has done, by the Marchi method and especially by the examination of the *boutons*. It is hoped, moreover, that one may some day have a clinical case in which the same method can be applied in tracing these important pathways.

Dr. Frederick Tilney, New York: I only want to say a word or two about the aberrant pyramidal cells in area 6. It has been my experience, after examining a large number of different mammals, both in the adult stage and also in that of ontogenesis, that many of the pyramidal cells from area 4 shift over into area 6, and I am perfectly certain from what I have seen that they belong to area 4 and not to area 6. Thus I think that in bringing out the evidence of these apparently pyramidal Betz cells in area 4 Dr. Fulton has simply emphasized a morphologic situation that occurs in nearly all mammals and the fact that these cells really belong to the true motor area.

Dr. John F. Fulton, New Haven, Conn.: The point Dr. Tilney raises is an important one. My co-workers and I had thought that the corticospinal degenerations in this area probably were due to destroyed Betz cells that had not become segregated from the motor area, and we believed that through superficial section of the cortex one would be likely to destroy the axons of those cells; we have reason to believe that they sweep backward in the superficial layers. Even with fairly deep incisions, however, we have been unable to remove them all, for subsequent removal of the premotor area itself gives rise to extensive corticospinal degeneration. Serial sections have in one instance revealed as many as 30 of the cells, and I should imagine that the degenerations that we are seeing affect 700 or 800 cells, as a rough estimate. We have as yet no accurate numerical count of the degenerating fibers.

HEART RATE IN RELATION TO EMOTIONAL DISTURBANCES

J. C. WHITEHORN, M.D.

M. R. KAUFMAN, M.D.

AND

J. M. THOMAS, M.D.

WAVERLEY, MASS.

We present in this paper certain of our observations on the heart rate under conditions designed to elicit emotional reactions. No explanation need be offered for investigating the emotions of psychotic patients. "Emotional reactions," "affective states" and other terms of similar connotation constitute a large part of the current psychiatric patter. In reading the psychiatric literature, one almost is led to think that a detailed knowledge of emotional conflicts would, in itself, be a knowledge of the causes of the psychoses. Some of our observations, however, appear to minimize rather than to emphasize the "emotional" significance of certain reactions.

We shall first present the observations descriptively and then discuss briefly their possible significance. The records represent the results of about two hundred and eighty hours of observation of forty-eight subjects, twenty-nine of whom were psychotic patients.

LITERATURE

A relationship between the heart and the emotions has long been known, but, without injustice to earlier workers, it may be said that serious investigation of the connection between organic processes and emotion began with the experiments of the Italian physiologist, Angelo Mosso,[1] in 1875. Since that date theories of affection and of emotion have inspired a multitude of experiments. Most of these have been so well summarized in the reviews of Angell and Thompson,[2] Stevens,[3] Shepard,[4] von Bechterew,[5] Darrow[6] and Boas and Goldschmidt[7] that

From the McLean Hospital.

1. Mosso, A.: Neben den Kreislauf des Blutes im menschlichen Gehirn, Leipzig, Veit u. Comp., 1881; Die Furcht, Leipzig, S. Hirzel, 1889.

2. Angell, J. R., and Thompson, H. B.: Psychol. Rev. **6**:32, 1899.

3. Stevens, H. C.: Am. J. Psychol. **16**:409, 1905.

4. Shepard, John F.: Am. J. Psychol. **17**:522, 1906.

5. von Bechterew, W.: Objektive Psychologie, Leipzig, B. C. Teufener, 1913.

6. Darrow, C. W.: Psychol. Bull. **26**:185, 1929.

7. Boas, E. P., and Goldschmidt, E. F.; The Heart Rate, Springfield, Ill., Charles C. Thomas, Publisher, 1932.

it seems superfluous to offer here another detailed review of the literature. It suffices to add that recent technical advantages have opened new avenues of approach to the study of the relationship between the heart and the emotions.

THE CARDIOCHRONOGRAPH

In planning and assembling the instrumental set-up which was used in the experimental study, we wished first of all to maintain for the subjects an experimental situation which would permit as close an approach as possible to the natural conditions of interpersonal relationships. Increasing experience has intensified the desire, for it has emphasized still more strongly the importance of the social aspect of emotional events. We likewise especially wished to avoid immobilizing the hands and arms of the subjects.

We have not, therefore, sought the most complete polygraphic methods of registering physiologic events; on the contrary, we have tried to devise a single method which, while unobtrusive to the subject, would record one of the well-established phenomena sometimes called the "physiologic expressions of emotion." For recording the heart rate we chose the Boas cardiotachometer.[8] In the use of this instrument, the contact with the skin of the subject is maintained by an elastic belt about the chest carrying two small, gold-plated electrodes from which a flexible cable leads to the instrument room. We use a paste made of a soap solution, fine sand and a little trisodium phosphate for the cleansing of the skin—the region over the apex of the heart being the area of contact for one electrode and an area in about the same relative position on the right side of the chest, for the other electrode. A little soft paste saturated with a solution of sodium chloride placed under each electrode maintains the electric contact. When the electrodes have been satisfactorily adjusted, the subject's clothing may be replaced. He is then free to stand, sit or lie down, to walk about the room or even to cross the hall, to be in a room alone or with another person, to play cards or to sleep—in other words, to escape many of the irritating, hampering and disturbing sensations of the usually cramped experimental situation. When a subject moves about his movements must, of course, be taken into account in the interpretation of the heart record. Some of our experiments on the effects of emotion have given ambiguous results on account of the physical activity of the subject at critical moments, but we have been willing to sacrifice a few records for the sake of a greater ease of attitude and naturalness of response on the part of the subject.

The leads from the subject, passing in a shielded flexible cable to the instrument room, are attached to the input posts of a Boas cardiotachometer, constructed for us by the General Radio Company of Cambridge, Mass.

For the purpose of the actual recording we were not satisfied with the devices commonly used with the instrument, either the method of continuous recording on a long strip or that of intermittent recording of the cumulative figures on a counting device. Dr. Boas told us of the instrument known as a *Zeitschreiber*, devised by Fleisch,[9] which we secured. This machine records graphically, as successive ordinates, the duration of rhythmically repeated cycles, such as those of the pulse or of the respiration. In the *Zeitschreiber*, a writing point is raised vertically (50 mm. per second) by a string of catgut over a pulley, connected through an electromagnetic clutch with a series of speed-reducing gears turned by

8. Boas, E. P.: The Cardiotachometer, Arch. Int. Med. **41**:403 (March) 1928.
9. Fleisch, A.: Ztschr. f. d. ges. exper. Med. **72**:384, 1930.

a constant speed motor. The opening of the electric circuit in the clutch releases the pulley of the writing point, so that the point may be quickly pulled down by a spring to the starting-point, and the closing of the circuit of the clutch causes the writing point to resume its upward climb at constant speed. The openings and closings are accomplished by a special wheel switch of constant speed which is caught or released by an electromagnet. The constancy of the speed of the wheel switch insures the constancy of the brief interval of time between the instant when the writing point ceases to rise (and begins to drop to the starting level) and the instant when it resumes its rise. With the particular instrument which we use, this "time out" was found, by records made with a tuning fork, to be seventeen-hundredths second. This interval must be added to the time represented by each ordinate to find the true duration of each heart cycle, or, more simply, a zero line may be drawn mechanically at just the proper distance (8.5 mm.) below the resting level of the writing point.

The degree of precision in the measurement of the time intervals by the *Zeitschreiber*, which is run by a direct current motor, the speed of which is regulated by a centrifugal governor, we determined by comparison with the vibrations of a tuning fork. The maximal error observed for a period of one second was fifteen-thousandths second; the probable error, four-thousandths second. We made it our custom to record for each experiment a series of one second intervals from a Harvard pendulum clock. The errors of the clock are greater than those of the *Zeitschreiber* for individual beats, but the general level is useful in confirming the position of the horizontal rate lines.

The writing point is arranged to write on stylograph paper which is drawn slowly (from about 2 to 3 cm. per minute) from a roll by an electrically operated kymograph. The kymograph is also provided with a minute marker and a signal marker to facilitate the correlation of events and with a scale which marks off for ease of approximate interpretation the heights of the ordinates corresponding to heart rates of 40, 60, 80, 100, 120 and 140 per minute.

The electromagnet which releases or catches the wheel switch of the *Zeitschreiber* is actuated in our set-up by the current through the output relay of the Boas cardiotachometer. In order to utilize the superior sharpness of the break, rather than of the make, of this delicate relay, we were obliged to alter the iron bar which catches and releases the wheel switch. (Fleisch's instrument was designed to be operated by a mercury-to-wire contact made by the radial pulse.) We substituted a bar on which the position of the two lugs is reversed so that the wheel switch is released and permitted to turn, thus breaking the circuit of the clutch and stopping the ascent of the writing point at the instant of the break in the output relay of the cardiotachometer produced by the amplified cardiac action current (the R wave). The instrument functions without this refinement, but with less precision, for the periods thus measured are not the intervals between the beginnings of successive heart beats but rather those between the instants at which the successive amplified cardiac action currents have died down to a certain level, the intervals depending somewhat on the degree of amplification. In many records the greater precision obtainable by the refinement is negligible, but the records of certain subjects would otherwise have contained variable errors of a few hundredths of a second per beat.

For convenience of discussion, this combination of cardiotachometer, *Zeitschreiber* and continuous kymograph may be termed a cardiochronograph.

The principal advantages of the cardiochronograph may be illustrated by the section of a record reproduced in figure 1. The lower line indicates the time expressed in minutes. The closely parallel vertical lines measure, beat by beat,

the duration of each complete cardiac cycle. The taller the vertical line,[10] the slower is the heart rate. When measured from the corrected base line, the series of vertical lines represent the successive time intervals which appear in an electrocardiogram as the successive intervals between R waves, but they are here brought together so closely that the equivalent information which would appear on nearly 5 feet (1.5 meters) of electrocardiogram is condensed into about 1 inch (2.5 cm.). The perspective so obtained throws into obvious and unmistakable relief two characteristics of the heart rate which lie unnoticed in the electrocardiogram or in the usual record obtained with a cardiotachometer.

The fact which first strikes the eye unaccustomed to this perspective is the unceasing variability of the heart rate. It is true that in certain subjects, under special conditions, a fair approach to a really steady rate may be maintained for several minutes, but the usual picture is one of successive phases of acceleration

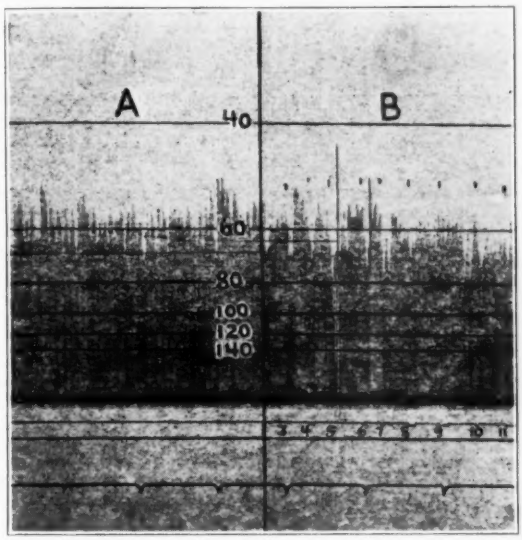


Fig. 1.—Record of the heart rate in a normal young woman, obtained with the cardiochronograph. Section *A* was obtained during a rest period; *B*, during a word association test. The lower line marks the time in minutes. The accessory horizontal lines marked *40*, *60*, *80* and so on indicate the level of the heart rate, expressed as the number of beats per minute, as recorded by the vertical lines.

and of deceleration. One's impression is closely analogous to that experienced at the first sight of brownian movements, when a bit of matter which seen macroscopically seems at rest is found on microscopic view to exhibit lively motions of its particles. The average constancy of the minute-to-minute count of the pulse is vividly appreciated as being merely the statistical resultant of a fluctuating equilibrium.

10. The movement of the kymograph was intentionally adjusted to bring the vertical lines so close together as to emphasize the upper margin rather than the individual upright lines. In the photo-engraved reproductions the individual lines are further blurred, but the height of the upper margin of the curve, which is the significant feature, remains distinct.

The second striking characteristic of the beat-to-beat variability of the heart rate as brought out by the perspective of this record is the tendency to slow abruptly and promptly and to speed up less quickly.

We first assumed that the beat-to-beat variability of the heart rate was a respiratory arrhythmia, but this has not been found true when checked against synchronized records of inspiration and expiration. It is possible by exaggerating the respiratory activity by breathing deeply and slowly to induce a regular respiratory arrhythmia, in which accelerations and decelerations of the heart rate are correlated with the breathing, but this is not the usual condition when the subjects breathe naturally and easily. We have evidence linking the beat-to-beat variability with psychologic events, but the presentation of the evidence follows more logically an account of the simpler attempts to study emotional reactions.

There are also incidental advantages in the cardiochronographic record. The cardiotachometer is by no means an infallible instrument. It may pick up and amplify electric action currents from the voluntary muscles of the thoracic wall. Even with the most careful adjustment, it may in certain subjects miss heart beats on occasion, for example, during deep inspiration. These artefacts are easily recognized in cardiochronographic records and therefore are not misleading, as they might be in the use of an automatic counter (fig. 1).

Among the disadvantages of our method may be mentioned the cord and belt, which prevent the subject from being entirely at ease. There is also a noise from the *Zeitschreiber,* which has been diminished by various devices but which has not been completely eliminated.

There are, of course, many other ways of recording the heart rate. By one method, fairly simple from the point of view of the subject, the electric changes from the heart are led off to an electrocardiograph. One of us (W.) has had experience with this method.[11] But to measure and plot the duration of each heart cycle from the electrocardiogram over a considerable length of time is extremely tedious. To transform one five minute electrocardiogram into a chart comparable to the direct cardiochronograph record required the continuous work of one man, with occasional assistance, for a ten hour day; this task is accomplished by our present set-up instantaneously and automatically. One need not wait until the next day to learn whether acceleration occurred during a particular conversation and just when and how it started and stopped. Using the cardiochronograph one may actually watch the record and guide the conversation in accordance with its indications.

EMOTIONAL DISTURBANCES

Our set-up enabled us to confirm the common belief that the heart rate may be markedly accelerated during an emotional experience. In some instances we used a so-called startling stimulus, such as the dropping of a weight, the breaking of a paper bag or a sudden gesture with the fist. In general, the subject immediately appreciated the artificiality of such a situation and experienced only a slight or questionable emotional change, and the heart record showed little if any deviation from its previous character. This type of experiment, however, has the advantage, when successful, of giving clearcut definition to measurements of the latent period.

---

11. Whitehorn, J. C.; Lundholm, H.; Fox, E. L., and Benedict, F. G.: New England J. Med. **206**:777, 1932.

We made attempts also at standardized accusations of crimes or of misdemeanors, but here again the artificiality was too readily recognizable to make it a dependable means of evoking emotion. Even our own earnest efforts to conjure up in the mind situations which we knew, if real, would be strongly emotional usually failed to produce a notable feeling, and likewise they produced only slight changes in the heart rate. We did observe, however, in this connection that the heart rate showed a considerably greater acceleration whenever the subject related to a companion what he was thinking of. (The effect of the merely motor activity of speaking, as determined by control experiments on indifferent material, is comparatively trivial.) This emphasizes the great affective importance of the situations existing between persons.

Our observations in reading experiments were also negatively significant. One of us, for example, while wearing the recording apparatus, read certain of the more pornographic selections in an unexpurgated translation of "Thousand and One Nights" in the search for something that might serve as a standardizable exciting stimulus, yet the record of heart beat was unusually steady, and the feelings likewise remained unperturbed. The critical, intellectual attitude tends to inhibit emotion. Indeed, one of our most effective means of obtaining a steady heart rate has been to provide the subject with reading-matter of moderate interest.

The most successful technic for the production of emotional disturbances and, correspondingly, of changes in the heart rate has been the conversational method—a "heart-to-heart talk." This is somewhat disconcerting to one's scientific tastes. A feasible standardizable means certain to evoke at will definitely recognizable emotions is desirable, as well as a sure method of preventing emotional reactions during control periods, but human beings appear to be too firmly individualized to permit of other than a highly personal approach. This method requires much note taking; a complete presentation of our material, therefore, requires a prohibitive amount of detailed description. We have carried out a considerable number of heart-to-heart talks with each other and with other subjects who were personally known to us. The cumulative evidence has been convincing that emotional disturbances, even of the moderate degree common in every-day life, quicken the heart. We present here a few specific incidents, more as illustration than as proof of this general statement.

The heart record obtained during one such incident is shown in figure 2, which is a six minute portion taken from near the end of a three hour record.

The subject, a normal young man well known to the observer, had been lying on a couch, sometimes alone in the room, sometimes talking with the observer. At the beginning of the particular period they were

talking about the subject's wife and his household arrangements. Reference had previously been made to a possible position outside the household which his wife was considering, and the talk had turned to the possible effect of the national election on the economic depression. His heart was beating fairly steadily at a rate of about 10 beats per minute faster than the basal rate. At the moment marked *W* the observer asked rather abruptly: "Just what kind of work will your wife be doing?" The subject explained that the proposed work was not really hard work but depended more on her personality. As he talked his facial expression was somewhat strained, his words were a bit jumbled and perspiration appeared on his forehead. As shown in figure 2, his heart rate was

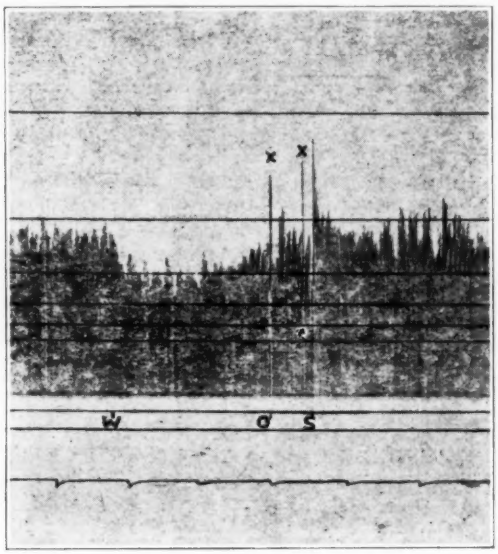


Fig. 2.—Six minute portion of the heart record of a young man, obtained during a conversational test.

accelerated for two minutes or so. The observer agreed that the work would be pleasant for her; he then excused himself and at point *O* in the record left the room, but he continued to watch the subject through a peep-hole. At no time in the period covered by this portion of the record were there noticeable movements of the body or limbs, except at the point designated by *S*, when there was a perceptible sigh, followed as usual by a sudden brief deceleration of the typical ratchet form, steeper on the left than on the right. (The two disturbances marked *x*, consisting of a slow beat preceded by a quick one, represent auricular extrasystoles.)

Other records of the usual simple emotional reaction are not presented; we wish, however, to show certain responses which, by reason

of their complications, have special points of interest. An illustration of such a response, involving several conflicting sentiments, is given in figure 3; this record was obtained from the same subject as figure 2, being taken about ten minutes previous to the latter. At the time marked *K* the observer said, referring to the wife's job, "Oh, yes, I meant to tell you that I spoke to Mr. K. yesterday about that arrangement." The subject's heart showed an extrasystole; the rate then accelerated moderately for three beats, then decelerated quickly and excessively and returned more slowly to the preceding rate. Meanwhile the subject had neither moved nor spoken, but his face wore for a moment what might be called a "nasty expression." At the time marked *L* he

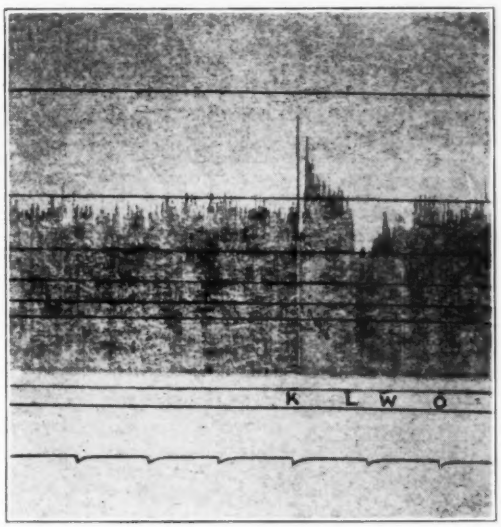


Fig. 3.—Portion of the heart record obtained ten minutes previous to that in figure 2 from the same subject during a conversational experiment.

said, "I didn't know whether to believe you or not," and this implied accusation of lying was followed by a clearcut acceleration. "Excuse me for my pessimistic idea," he added; then at the point marked *W*, he explained, "I had an idea you said that just to obtain a reaction." He paused about a half-minute, while his heart went through a sequence of minor accelerations and decelerations; he then added calmly and with the intonation of a question, "Otherwise, I should have asked you what the outcome was."

One can trace in this conversation the subject's secondary rejection of an emotionally disturbing topic, which was correlated with a marked deceleration, and then his fairly frank, but somewhat distressing, accusation of dishonesty, accompanied by considerable acceleration, which was cleared by an apology and explanation.

Another incident, for which there is no record, illustrates a similar acceleration, marked but brief, at the moment of emotional disturbance and the abrupt slowing which may occur in the heart's action when the so-called "overt expression" of emotion appears. The subject was a paranoid schizophrenic man of long hospital residence who had, however, retained remarkable intellectual interests and aptitudes and who had been for a short time under psycho-analytic study. During the experiment he was lying quietly on a couch talking with one of us (K., who had been his analyst) as he repeated the story of his first personal acquaintance with Jehovah—how Jehovah had appeared to him, part man, part woman, and in some respects like his father. He stated that he (the patient) and Jehovah had "conjugated, part to part, body to body, brain to brain and cell to cell." His heart rate, moderately variable, was then about 78. The interviewer inquired what the patient meant by "conjugation," whether it implied a homosexual relation to the father. The patient's heart rate became accelerated to 98 for about one quarter of a minute; he then spoke angrily, "I think you've been studying Freud only as a diseased mind might do." Here he sat up. "A remark like that wouldn't give one much respect for Freud." Meanwhile, his heart rate during the "expression of anger" had decreased to 75, in spite of the motor activity and the change of posture. He then stood up and, gesturing with his arms, launched into a vehement denunciation of "filthy freudianism." His heart rate momentarily reached 90 and then fluctuated in the vicinity of 80 but did not again reach 98. In a few minutes he was again pleasant and courteous.

This incident illustrates how relief from an emotional disturbance may be obtained by utilizing a motor pattern of "expression" and also how the heart record may reflect the sequence of events in spite of the contrary tendency to acceleration introduced by the actual motor activity.

We have several records made in cases of "agitated depression" which show a similar slowing and also a steadying of the heart rate as the patient swings back into the accustomed condition of motor agitation and habitual verbal self-accusation after a momentary deflection to a really more disturbing train of thought. Indeed, we have obtained some of the records showing the steadiest heart rates from patients of the agitated-depressed type at times when they were displaying the typical hand-wringing, quasiemotional behavior. An incident of this kind is illustrated in figure 4.

The subject was an unmarried woman of 64, depressed, agitated and self-accusatory, whose twin sister, also a patient in the McLean Hospital, had a similar psychosis. She had been complaining that the observer would go to the gymnasium and tell everything he had found out about her in the test, so that all the world would know it and her sister would find it out. At the moment marked *4* the observer asked, "Do you wish

her [the twin sister] to leave the hospital?" The patient said, "No, no, no!" and shifted about on the couch. "It's all my fault. We haven't any home to go to. . . . The home is all broken up." At signal *5* the patient continued, while rubbing the side of her face with her hand: "Oh, good God, the misery, the agony I've brought on this world." She went on, biting at her finger: "It's in all of the papers. . . . Wars. . . . Disasters. . . . Murders. . . . Oh, good God!" Meanwhile her heart, recovering from the disturbance at *4*, was remarkably steady. At *6* the observer interrupted the performance by asking, "But your sister, how about her?" The heart rate momentarily accelerated

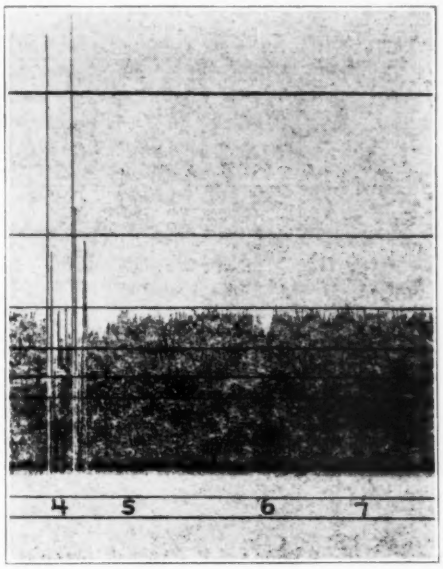


Fig. 4.—Portion of the heart record of a psychotic patient of the "agitated-depressed" type, obtained during a period of agitation.

as the patient said: "She is in hell. I sent her there." Then her heart rate became slower and was steady again as she continued: "I've made a hell for other folks. Oh, God! I'm very much afraid. . . . I've made life a hell for other folks. . . . Oh, the misery and the agony I've caused," and so on.

The few cases just presented not only illustrate the most common observation, that is, that of the acceleration of the heart rate which occurs at moments of emotional disturbance, but give a conception of the combination of acceleration and deceleration which may appear in complicated reactions. We have been especially interested in studying these cases for the information which they give concerning the psychophysiologic organization of sentiments. Even without further detailed

discussion, it is evident that the emotional disturbance and cardiac acceleration evoked by the conversational method are not produced by purely innate reflexes, for the dependence on the topic of conversation is in itself sufficient proof that one is dealing with ontogenetically developed responses—in neurologic terms, that the heart is controlled through the cerebral cortex, whatever other links may appear in the chain.

STUDIES OF WORD ASSOCIATIONS

The difficulties of recording and of timing a heart-to-heart talk led us to try the procedure of word association, primarily as a skeletonized conversation capable of fairly sharp synchronization with the heart record.

A prepared list of words is read, one at a time, by the experimenter, and the subject is instructed to respond to each word by speaking whatever word comes to mind. A signal circuit is closed at the last syllable of the stimulus word and opened at the beginning of the subject's response, thus registering on the heart record the time required for the exchange of words.

Ordinarily the heart rate is appreciably faster (by 5 or 10 per cent) during the reading of the entire list of words than in the preceding rest period, and this general acceleration is more marked during the first minute or two. Usually on examining the record one finds well marked accelerations associated with personally significant word exchanges, such as "hotel-honeymoon" in the case of a recently married subject. Some of the subjects show few changes in heart rate during the test; others show definite accelerations, often one and sometimes two extra beats, for each stimulus word given. The latter type of person may also show frequent brief accelerations when left alone and without stimulus words. In our efforts to find the explanation for these observations, we have given most serious consideration to two contradictory possibilities: First, that the brief accelerations of the heart occur at moments of special emotional tension in one's train of thought, in which case the observer should be able to demonstrate systematic time relationships when the course of thought and feeling is brought under experimental control by the word association, skeletonized type of conversation; second, that the accelerations of the heart have nothing to do with psychologic events, in which case they should show no systematic time relationship to stimulus words in the skeletonized conversation.

The experimental check of these possibilities is not decisive in its results in the subjects who take the word association test with indifference and who respond in such a glib and careless fashion that the word exchanges exercise little control over the course of thought. Other subjects take the test more in earnest. A record obtained from one of the earnest type is presented in figure 1. This subject, a nurse, had

to pay careful attention because she was not yet thoroughly familiar with the English language. We may take her record as an example of that of a person whose course of thought is held closely to the word exchanges. Section *A* in the record is taken from a resting period, and *B* is a section from the period of the word association test. Short, sharp accelerations are common events in both, but they are more marked in *B*. What is more significant, accelerations are found to occur just after the presentation of the stimulus words with a regularity about six times that which could be attributed to pure chance. Among the records from the word association tests that we have accumulated to date this type of response is most common. Another type of subject shows accelerations more regularly associated with his own responses than with the stimulus words. One man, when subjected to his third word association test and while responding to it glibly, showed a few accelerations in heart rate but they were regularly associated neither with the stimulus nor with the response words.

In general, however, the evidence so obtained indicates that the sudden brief accelerations which appear in many records are closely related to the course of psychologic events. Whether the similar accelerations observed when the subject is left to his own thoughts are likewise thus related is difficult to determine by experiment, since it is not possible to induce a psychologic vacuum for purposes of comparison.

Incidentally, the combination of the recording of the heart rate with the word association test has provided results which are of considerable interest in the analysis of personal problems and in the characterization of personality.

During the detailed study of the records we have been led to attach an unexpectedly great significance to the latent period between the stimulus and the acceleration. There is a definite tendency for the acceleration to appear and to reach its maximum within three or four seconds of the word stimulus. Of 333 measurements, in only one fifth did the period preceding the maximum acceleration exceed four seconds. Incidentally, in the particular records on which the 333 measurements were made, there were 358 word exchanges. Ninety-three per cent of the stimulus words were followed by definite accelerations, and of these more than 80 per cent were within four seconds. With a sudden startling stimulus of brief duration, such as the breaking of a paper bag, an acceleration usually appears within the time of one heart beat. The precise time in fractions of a second is perhaps not so significant as is the comparison of this with the much longer latent period (of about usually ten seconds) which has been determined by physiologists as that required for the acceleration of the mammalian heart by way of the sympathetic nerve supply.[12] By this criterion, one infers that the emotional accelera-

12. Hooker, D. R.: Am. J. Physiol. **19**:417, 1907.

tion of the heart rate is produced by the inhibition of the vagus center and not by the excitation of the sympathetic, just as Reid Hunt [13] concluded from similar evidence that the reflex acceleration of the dog's heart is caused by central inhibition of the vagus and as Gasser and Meek [14] stated that the sudden acceleration at the commencement of exercise is negotiated through the vagus. One uncertainty remains in this line of evidence, namely, whether or not in man, as in some other mammals, acceleration through the sympathetic has a relatively long latent period. We wish that a surgeon who has access to the thoracic cavity would resolve this doubt. The evidence indicating inhibition of the vagus as the mechanism for the emotional acceleration of the heart provides a way out of a theoretical difficulty. One of us (Dr. Whitehorn [15]) reported recently the negative results of a rather long and thorough search for emotional hyperglycemia. The rarity or absence of hyperglycemic responses in human emotions inclines one to doubt the activity of the thoracic sympathetic system in such states. The occurrence of cardiac accelerations as a regular concomitant of human emotions, even when of moderate intensity, might appear at first thought to indicate that the thoracic sympathetic system is activated in the cardiac effector portion while suppressed in the suprarenal effector function—an assumption which contradicts the general tendency of the thoracic sympathetic system to act *en masse* in its effector functions. This improbable hypothesis need not now be proposed, for our observations on the brevity of the latent period of accelerations psychologically induced indicate that the accelerations may be negotiated through the vagus. We cannot, however, state definitely that this nerve always furnishes the mechanism, for in many of the emotional reactions obtained by the conversational method latent periods cannot be measured because the moment of stimulation cannot be exactly specified.

Certain other physiologic concomitants of emotion appear in the organs which are antagonistically innervated by the parasympathetic and the sympathetic system, such as the iris and the gastro-intestinal canal. It would be interesting, if possible, to determine whether the emotional effects on the organs are accomplished through inhibition of the parasympathetic innervation or through excitation of the sympathetic system.

ACCELERATIONS ASSOCIATED WITH PHYSICAL MOVEMENTS

Although we were primarily interested in the psychologic correlations, we have been compelled to give close attention to the changes in heart rate associated with physical movements, simply as a necessary control, for we wished to guard against the possibility of attributing to emotion

13. Hunt, Reid: Am. J. Physiol. **2**:395, 1898-1899.
14. Gasser, H. S., and Meek, W. J.: Am. J. Physiol. **34**:48,1914.
15. Whitehorn, J. C.: Am. J. Psychiat. **13**:987, 1934.

changes produced by motion and vice versa. We have made no special studies on prolonged or excessive physical work, with the exception of one experiment in which an emotional stimulus was introduced during strenuous exercise. Even though the exercise had increased the heart rate from about 80 to over 120 per minute and was maintaining it at that level, the emotional disturbance produced a definite further acceleration. We have accumulated, however, a considerable number of observations on moderate or slight physical activity and on posture.

In moderately vigorous physical exertion, such as stepping up and down on a chair five times in fifteen seconds, the heart rate increases rather slowly (sometimes being hardly noticeable before the exercise is over); the acceleration outlasts the exercise (usually reaching its maximum afterward) and returns gradually to the general level. This course of events parallels fairly closely the requirements of the tissues for oxygen.

The changes in heart rate which occur when the subject stands up or lies down are almost instantaneous, as regards the major portion of the change. The faster rate on standing and the slower rate on lying down may well provide for the different oxygen requirements in these postures, but the greater portion of the change occurs before the difference in the rate of consumption of oxygen could be effective, and the promptness in response inclines one to suppose that it is brought about by sudden reflexes through the mechanism of the vagus. Another effect of posture is also out of line with the explanation of the requirement for oxygen, namely, the slowing of the heart rate when the standing subject leans forward. The heart rate is frequently slowed as much as 20 per cent by this change, whereas the oxygen requirement must be considerably increased by the muscular effort involved.

When the subject is lying down, a change in the position of the body or a movement of the limbs is correlated with a change in heart rate, nearly always with an acceleration. If the chest is turned there is also, usually, a subsequent deceleration. Such changes are often strikingly abrupt, and we have frequently observed that the acceleration begins before the movement. The degree of acceleration bears little if any relation to the amount of physical motion. For example, one subject whose record is given in part in figure 5 was lying on a couch, alone in the room, but was aware of being observed and was fidgety. At *A* he moved the head; at *B*, both legs; at *C* he did nothing more than wink the eyes in a manner familiar to us as a habitual tic; at *D* he moved the left arm, and at *E* he shifted the whole body. The acceleration associated with the winking of the eye was just as marked as that with the other movements.

The same degree of slight physical activity may be associated at one time with a considerable acceleration and at another with none,

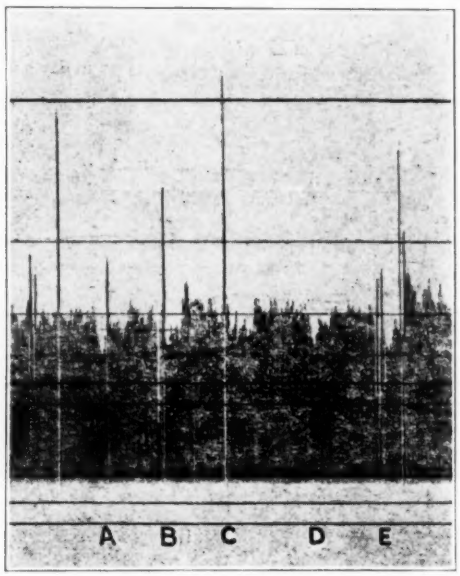


Fig. 5.—Section of the heart record of a nervous subject, showing the accelerations in the heart rate during various physical movements, regardless of their magnitude.

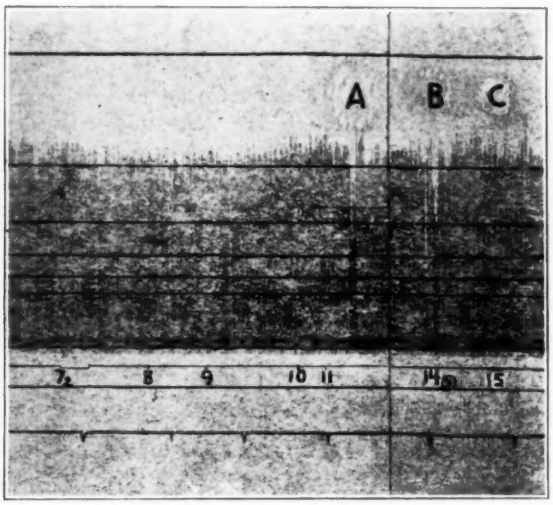


Fig. 6.—Heart record of a man, showing accelerations in the rate which accompanied movements performed under command and their absence with movements performed without excitement.

depending on the circumstances. In the subject part of whose record is shown in figure 6, the acceleration recorded at *A* occurred when he raised the right hand from his side to his head and put it back again. This movement had been repeated several times during the record with accompanying accelerations. At *B* the subject was rather abruptly commanded, "raise your right hand to your head and put it down again." This performance, which was executed immediately, was also accompanied by an acceleration. The subject was then asked to repeat the movement at any time he wished during the next minute. When he did so, at *C*, there was no definite acceleration.

It seems to us on the basis of these and many similar observations that the sudden accelerations associated with small, spontaneous and fidgety movements are probably emotional in origin and that the same explanation may hold for similar movements executed on direct command.

DECELERATIONS

In order to restore the regular rate, it is obvious that the heart must beat more slowly after an acceleration or that it must accelerate after each deceleration, depending on one's point of view. In the actual observation of the records, however, there is seldom any ambiguity about the sequence. The regular fluctuation of rate, when the subject is in a relatively quiet period, follows a fairly stable pattern. An acceleration occurs, followed immediately by a deceleration, which is usually more rapid than the acceleration. Then after a variable time another sequence of acceleration and deceleration occurs. A deceleration may occur without an immediately preceding acceleration but it rarely does. The visual impression is strong that the decelerations represent the positive action of a brake. The neural mechanism involved must be the vagus for the decelerations are too sudden to be attributed to the inhibition of the sympathetic nerves or to humoral agents coming from distant organs.

It is by no means rare for the duration of the heart cycle to increase abruptly by as much as 40 or 50 per cent, and sometimes by almost 100 per cent within the time of one beat. We have given much attention to decelerations of this striking type, but we have not arrived at a completely satisfactory formulation of the conditions in which they occur. Many of our observations point to an association with feelings of disgust—both in the sense of a definite nausea, with or without retching or vomiting, and also in the more attenuated sense of rejection, aversion or resignation.

The two types of experience associated with striking deceleration are illustrated by the following examples: In one case a man (non-psychotic), who commonly has sick headaches after smoking, smoked

two cigarets in succession, fairly rapidly. A headache promptly developed, and he became nauseated in waves about one minute apart; the heart record, which in the preliminary period had been fairly steady, showed in general a faster rate, punctuated by increasingly large abrupt decelerations which coincided fairly closely with the waves of nausea. Finally, after about five minutes of increasing nausea and increasing peaks of deceleration, he vomited. The nausea ceased, and so did the decelerations, although the headache continued. In the other experiment, one of us, after sitting as a subject before the recording device and waiting for decelerations to occur in an effort to find by introspection a clue to their psychologic significance, "gave up in disgust," only to be rewarded at once by a beautiful deceleration.

We list under the similar general category of disgust or aversion a number of other experiences found to be associated with striking decelerations. For example, one subject in an experiment with word associations accompanied each response to a "nasty sex word" by a marked deceleration. The only other deceleration of marked degree during the test was one in response to the word "socialist," which also, from our personal knowledge, we judge was for him a "nasty" word.

In one of our subjects who was frequently studied and who was susceptible to intestinal disturbances, sudden excessive decelerations were common and appeared most frequently on days when he had considerable abdominal distress, which suggests a reflex basis. Nevertheless, on one such occasion a simple reading experiment almost completely eliminated the peaks of deceleration. Observations of this kind, suggestive of a correlation between the state of mind and the alternate inhibition and excitation of the vagus, both in its cardiac and in its gastro-intestinal distribution, lead also to a rather far-fetched suggestion that peptic ulcers may be produced or aggravated by the types of mental reaction that induce sudden decelerations of the heart. We have no direct evidence for this hypothesis, but even the possibility of its truth has added interest to the search for the psychologic meaning, if any, of abrupt decelerations.

In some subjects a sigh almost invariably produces a marked deceleration, the rate changing from about 80 or 90 to 50 or 60 per minute within the time of one beat and then steadily accelerating within a period of from a dozen to twenty beats to the previous level. Sudden decelerations have also been observed at times when the attention is suddenly turned from one topic or person to another—as one of the sensitive subjects said, "when I get my mind off myself." We have had two schizophrenic patients, dilapidated and superficially apathetic but with persistently rapid heart rates, who showed brief, abrupt decelerations when an observer came into the room and sat down.

GENERAL COMMENT ON EMOTION AND BEHAVIOR

Whoever at the present time deals with the study of emotion finds it extraordinarily difficult to present conclusions or results in terms which are generally understandable or are clear in meaning. In the discussion of most matters it is the wisest policy to draw one's vocabulary and definitions from the so-called academic sources, for it is in the schools and in the universities that the terms used in the transmission of knowledge receive the most careful attention. But when one seeks academic guidance in the systematic discussion of the problems involving emotion, one finds no generally accepted system of definitions. One need only read the reports of the Wittenberg symposium on this topic [16] to be convinced of the lack of a common basis of understanding.

With respect to one of the conflicts in the present-day confusion, namely, the tendency, on the one hand, to delineate a number of specific emotions and that, on the other hand, to emphasize the general, rather than the specific, character of emotion, the results of the study reported here incline us strongly toward the latter view. In all of the experiments in which we had good reason to think from our own introspections or from the introspective reports of reliable subjects that a considerable disturbance of the subject's equanimity occurred there was recorded, at the beginning of the disturbance, an acceleration of the heart rate. The acceleration was followed by increasing acceleration, by gradual slowing or by sudden excessive deceleration, and the psychologic experience was variously described, but there was uniformly present at the beginning a period of quickened heart rate.

We have not been especially interested in trying to identify and describe "specific emotions" either in psychologic or in physiologic terms. It seems most probable from Brunswick's report [17] and from the photographic studies of Landis [18] that there are no physiologic patterns of activity characteristic of the "specific emotions," even if such entities exist. Our own point of view in the matter is based on general experience rather more than on specific experiments. To us it appears unfortunate that so much credence has been given to the hypothetic psychologic entities assumed to underlie the distinguishable types of behavior, facial and otherwise, which have been described as the "expressions" of the hypostasized emotions. It is our opinion, though not at all original with us, that the activities, sometimes labeled in a pseudosophisticated way as "expressions" of a hypothetic specific "emotion," may be dealt with to greater scientific advantage if considered simply for what they are, namely, action patterns. As action patterns, they have many interesting aspects. Not the least interesting

16. Wittenberg Symposium, Worcester, Mass., Clark University Press, 1928.
17. Brunswick, D.: J. Comp. Psychol. **4**:225, 1924.
18. Landis, C.: J. Comp. Psychol. **4**:447, 1924.

is their employment as social gestures, by which persons reveal to, or, it may be, conceal from, each other their attitudes and inclinations of behavior. The so-called "expressive" action patterns are also linked into the more complex psychophysical dispositions to which the term "sentiment" is aptly applied. But we are of the opinion that it is distinctly advantageous to reserve the term "emotion" for the nonspecific condition of a disorganizing, upsetting, confusing disturbance of equanimity. It is in that sense that we use the word "emotion." If we correctly understand Gantt's translation of Luria's treatise,[19] we agree with him in this definition.

This usage of terms permits us to condense much of our experience into the statement that cardiac acceleration is, as a rule, found in emotion. If, then, acceleration is considered tentatively as the indication of emotion, an emotion frequently appears to be promptly resolved rather than to be intensified when the subject shows some one of the action patterns commonly considered as the "expression" of a particular "emotion," such as anger or grief.

Our experiences with psychotic patients have provided a number of incidents to exemplify the slowing and steadying of the heart rate coincident with the so-called "expressive" action patterns. In some instances this was as expected from simple clinical observation, for every psychiatrist is familiar with the patient whose show of emotion seems hollow and theatrical. Some patients even state that they no longer experience emotions. But the apparently incongruous slowness and steadiness of heart rate are not limited to the fairly obvious cases of pseudo-emotional display, and even then these persons do not always maintain an impervious equanimity, as illustrated in the heart record in figure 4. As a result of our experience it seems that in order to detect by direct observation of the patient that emotional disturbance (as we have defined it) which coincides with acceleration in the heart record, one's best method is to watch the patient's face and limbs for confused, hesitating or conflicting activities rather than for smoothly executed, nonambiguous patterns. The accumulated weight of this experience, which is rather difficult, it is true, to put into precise descriptive language, has strongly influenced us to take the position already expressed that the overt action patterns when clearly patterned are better understood as social gestures than as "expressions of an emotion." It is, perhaps, not feasible to abandon the use of such terms as a "facial expression of anger." It may be used as a short and summary statement of observations, somewhat as one may say, "I saw the sun come up at 6 o'clock this morning," well knowing that this is not an exact statement of the relative motions of the sun and earth.

19. Luria, A. R.: The Nature of Human Conflicts, translated by W. H. Gantt, New York, Horace Liveright, Inc., 1932, p. 169.

Furthermore, when one tries to be more discriminating and call these "expressions" gestures it is not implied that they are necessarily insincere or even that they are used always with the full and deliberate intention of communication, any more than other means of social communication, such as words, are so used. But even when sincere and unintentional, the clearly patterned social gesture "expressive of an emotion" seems to "take the edge off" the emotional intensity and at the same time to slow the heart rate.

SUMMARY AND CONCLUSIONS

A recently developed apparatus, the cardiochronograph, combining the Boas cardiotachometer and the Fleisch *Zeitschreiber,* makes it possible to record the time of each heart beat over long or short periods in a perspective which throws into graphic relief the almost ceaseless fluctuations in the heart rate.

Illustrative examples are presented from records of the results of about two hundred and eighty hours of observation, of forty-eight subjects, twenty-nine of whom were psychotic patients.

To judge from introspective observations and from the results of word association experiments, the brief accelerations which frequently appear in many of the records seem to occur at moments of fleeting emotion. More profound emotional disturbances elicited by heart-to-heart talks give more marked cardiac accelerations, which may persist, may be slowed gradually or may be terminated by abrupt, excessive decelerations, depending on the subject's mode of action. Abrupt decelerations are mediated through the vagus nerve, and many accelerations appear also, by reason of the short latent period, to be negotiated through the release of vagus inhibition rather than through sympathetic excitation.

Our experience with psychotic subjects indicates the great need for caution in the psychologic interpretation of so-called emotional behavior. Action patterns commonly taken as overt expressions of the hypothetic "emotions" are more advantageously considered simply as action patterns indicative of attitudes, habits and inclinations of behavior. Much of what appears as "affective" behavior has rather the significance of social gestures.

NEUROLOGIC ASPECTS OF THE EPIDEMIC OF ENCEPHALITIS IN ST. LOUIS

J. WILLIAM BECKMANN, M.D.
Instructor in Neurology and Psychiatry, Washington University Medical School
ST. LOUIS

In July 1933 about 13 cases of encephalitis of an unusual type occurred in St. Louis, ushering in an epidemic. In August, 527 cases were reported; in September, 444, and in October, 58. Cases were first seen in St. Louis County, and later the disease spread into the city. The total number of cases reported was 1,097. The clinical picture was unlike that presented in other types of encephalitis in this country in that (1) the seasonal incidence, namely, its occurrence in the hot summer months, distinguished it from typical epidemic encephalitis, which occurs during the winter, (2) the illness caused a marked constitutional reaction but ran a shorter course and (3) while the general population was affected, the incidence in persons over 40 years of age was greater.

In retrospect, typical cases of encephalitis had been seen in the community many months previously. Two will be cited.

CASE 1.—J. M. J., a boy, aged 16, who was seen on Dec. 10, 1932, had had a sore throat and general malaise two days before, and on the next day had severe pain in the nose and in the roof of the mouth. He became suddenly unconscious, while at dinner, and was brought to the hospital. When first seen he was delirious, thrashing about in bed and becoming excitable and almost unmanageable when any attempt was made to examine him. The throat and tonsils were injected.

The neurologic examination showed some stiffness of the neck, sluggish deep reflexes, absence of abdominal reflexes on the left and a Babinski sign on the right. The eyegrounds were normal. The white cells of the blood numbered 9,650, with 37 per cent lymphocytes. The pressure of the spinal fluid was somewhat increased; a cell count revealed 5 lymphocytes per cubic millimeter; smears and cultures gave negative results. The temperature rose from 99 to 102 F. for two days and then fell to 100 F. In the meantime, neurologic examination had shown a Rossolimo sign on the right; the abdominal reflexes had disappeared; the knee jerk was increased on the right; mentally, the hyperactive delirious state had decreased, but the patient still showed drowsiness and confusion.

A diagnosis of pansinusitis was made by a rhinologist, and treatment was administered for this condition. The patient improved rapidly; all the abnormal neurologic signs disappeared, and he was discharged at the end of ten days, feeling well.

CASE 2.—M. B., a married woman, aged 40, was seen on Jan. 12, 1933; a relative said that for the previous three days she had terrific headaches which did

---

Read at the Sixtieth Annual Meeting of the American Neurological Association, Atlantic City, N. J., June 5, 1934.

not respond to medication, that she had been unable to sleep for two nights and that on January 10 she lapsed into a state of drowsiness and failed to respond to questions or to take food.

When first seen the patient was in a stupor. The head was extended and turned to the left. There were extreme rigidity of the neck and a positive Kernig sign. There was conjugate deviation of the eyes to the left. An ophthalmoscopic examination showed only overfilled veins. The corneal reflex was absent on the right. There was central facial weakness on the right side. All the deep reflexes were absent. The Babinski sign was positive on both sides. An examination of the chest gave negative results. The blood pressure was normal. A white cell count showed 11,300 cells, with 83 per cent polymorphonuclears and 13 per cent lymphocytes. A lumbar puncture, although easily made, showed bloody spinal fluid, the amount of blood remaining the same in all the specimens. A microscopic

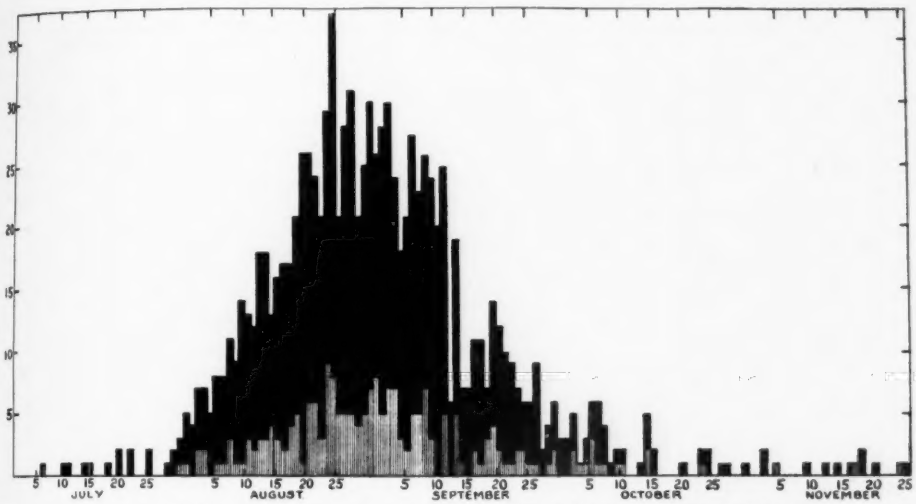


Chart 1.—Daily incidence and mortality in the epidemic of encephalitis in St. Louis. The black areas indicate the total incidence; the shaded areas, the mortality.

examination showed no crenated cells, and bacteriologic tests and inoculation of animals gave negative results.

Signs of a lesion of the pyramidal tract developed rapidly. The left arm became flaccid and then slightly spastic; in the latter stage a grasp reflex was elicited. The pupils showed transient variations in size. Further lumbar punctures yielded bloody spinal fluid. The temperature ranged from 101.6 to 103.8 F., and the pulse rate, from 80 to 150. The patient died on January 18. Autopsy was not permitted.

This apoplectiform type of picture, associated with signs of meningeal irritation and bloody spinal fluid, was seen in two other other patients aged between 40 and 50 years, who showed no evidence of arteriosclerosis, hypertension or cerebral hemorrhage. Cases of lymphocytic meningitis or serous meningitis had been observed previ-

ously, but clinically the patients seemed less ill and recovered. These cases also differed clinically from those of tuberculous meningitis in that the onset was acute and fulminating and the course was short. For these reasons, it is likely that these cases were probably forerunners of the encephalitis seen in the epidemic. Neutralization tests in the first case substantiated this impression.

A comparison of the encephalitis observed in the St. Louis epidemic with other forms of encephalitis seen in epidemics, namely, the true epidemic type and the Japanese type, or encephalitis B, brings out the following points: 1. A close correlation existed in the seasonal incidence between this epidemic and the Japanese epidemics of 1924 and 1927, 1928 and 1929. 2. A large proportion of cases of the typical epidemic type have occurred in patients under 20 years of age, while in both

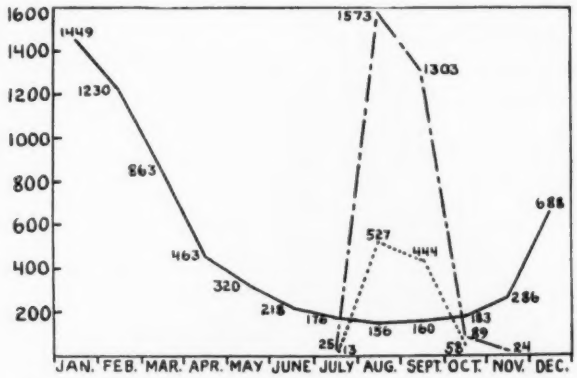


Chart 2.—Seasonal incidence of encephalitis in epidemics. The solid line indicates the seasonal incidence for 7,876 cases of epidemic encephalitis reported in the literature; the dotted line, the incidence for 1,097 cases in the epidemic of 1933 in St. Louis; the dash-and-dot line, the incidence for 3,118 cases in the Japanese epidemics from 1927 to 1929.

the Japanese and the St. Louis types the disease occurred with increasing frequency in patients over 40. An analysis of the figures reduced to percentage of the population shows no particular incidence according to sex or race.

The mortality rates, however, show marked differences. In 23,567 cases of epidemic encephalitis, the mortality rate was 47.8 per cent, the highest number of deaths occurring in the age group between 1 and 10 years and a comparatively large number in that between 36 and 55 years. The mortality in the Japanese epidemic of encephalitis for the years 1927, 1928 and 1929 was 66.9 per cent, with a progressive increase in the rate from the age of 50 on. In the epidemic in St. Louis the mortality rate was 20.1 per cent, with an increasing incidence from

TABLE 1.—*Age Incidence and Mortality Rates in Various Epidemics of Encephalitis* *

	Epidemic Encephalitis†				Japanese Encephalitis‡				St. Louis Encephalitis§				
Age Group, Years	Number of Cases		Deaths		Percentage of Mortality		Age Incidence, Years	Number of Cases	Deaths	Percentage of Mortality	Age Incidence, Years	Number of Cases	Deaths	Percentage of Mortality	
1	12		9		75.0						0- 1	6	1	16.7	
1- 5	74	181	50	104	67.5	57.45	0-10	379	184	48.55	1- 4	32	3	9.4	8.04
5-10	95		45		47.3						5- 9	49	3	6.1	
10-15	151		50		33.1						10-14	44	—	0.0	
15-20	176	327	74	124	42.0	37.67	11-20	307	160	52.12	15-19	59	4	6.2	3.87
20-30	191		80		42.1		21-30	232	128	55.17	20-29	135	5	3.7	
30-40	193		93		47.8		31-40	228	132	57.89	30-39	131	10	7.6	
40-50	187		94		50.0		41-50	262	156	59.54	40-49	173	21	12.1	
50-60	121		72		59.5		51-60	416	297	71.39	50-59	174	37	21.2	
60-70	57		36		63.3		61-70	609	454	74.54	60-69	183	70	38.2	
70-80	15		12		80.0		70-	685	577	84.23	70-79	91	51	56.0	
											80-89	20	16	80.0	60.36
All ages	1,272		615		48.35			3,118	2,088	66.96		1,097	221	20.1	

* Matheson Commission: Epidemic Encephalitis: Etiology, Epidemiology, Treatment, New York, Columbia University Press, 1929; Second Report, 1932.

† The figures for epidemic encephalitis are from Parsons, A. C.: Report on Encephalitis Lethargica, Great Britain Ministry of Health, Reports on Public Health and Medical Subjects, no. 11, London, His Majesty's Stationery Office, 1922.

‡ The figures for Japanese encephalitis are from Health Bulletin 1751, Department of Public Health, Tokio, Japan.

§ The figures for St. Louis encephalitis are from the Department of Vital Statistics, St. Louis.

TABLE 2.—*Incidence and Mortality Rate According to Age, Sex and Color in the St. Louis Epidemic of 1933*

Age Group, Years	Total Number of Cases	Number of Deaths		Percentage of Mortality		Males	Number of Deaths	Percentage of Mortality	Females	Number of Deaths	Percentage of Mortality	Number of White Patients	Number of Deaths	Percentage of Mortality	Number of Colored Patients	Number of Deaths	Percentage of Mortality
1	6	1		16.7		4	1	25.0	2	..	...	6	1	16.7	..	..	...
1- 4	32	3	87	9.4	8.0	21	1	4.8	11	2	1.8	23	2	8.7	9	1	1.1
5- 9	49	3		6.1		31	2	6.5	18	1	5.6	39	3	7.7	10	..	...
10-14	44	..		...		28	..	...	16	..	...	41	..	...	3	..	...
15-19	59	4		6.2		22	..	...	37	4	1.8	50	2	4.0	9	2	2.2
20-29	135	5		3.7		53	3	5.7	82	2	2.4	119	4	3.4	16	1	6.3
30-39	131	10		7.6		61	5	8.2	70	5	7.1	121	9	7.4	8	1	12.5
40-49	173	21		12.1		88	14	15.9	85	7	8.2	156	16	10.3	17	5	29.4
50-59	174	37		21.2		92	21	22.8	82	16	19.5	156	30	19.4	18	7	38.9
60-69	183	70		38.2		86	34	39.5	97	36	37.1	169	64	37.9	14	6	32.8
70-79	91	51		56.0		39	24	61.5	52	27	51.9	87	47	54.0	4	4	100.0
80-89	20	16		80.0		14	12	85.7	6	4	66.7	19	15	78.9	1	1	100.0
All ages	1,097	221		20.1		539	117	21.7	558	104	18.6	988	193	19.5	109	28	25.7
City	577	130		22.58		279	69	24.75	298	61	20.44	502	114	22.7	75	16	21.35
County	520	91		17.50		260	48	18.46	260	43	16.54	486	79	16.25	34	12	35.25

the age of 50 on. Therefore, the general incidence and mortality in the epidemic of encephalitis in St. Louis correspond in a reduced degree to those observed for the Japanese type.

Because of similarities in seasonal and age incidence, and in the mortality rates as based on the patients' ages, a comparison of the clinical findings in the epidemic in St. Louis with those in the Japanese epidemic is interesting. In both epidemics the disease ran a more acute and stormy course and was of much shorter duration than typical epidemic encephalitis. Pathologically, also, the microscopic picture of lymphocytic infiltration, with cuffing of the vessels, areas of hemorrhage and degeneration of ganglion cells throughout the brain, was found in both types. However, in the Japanese type areas of necrosis were numerous and striking. Such manifestations of acute invasion made

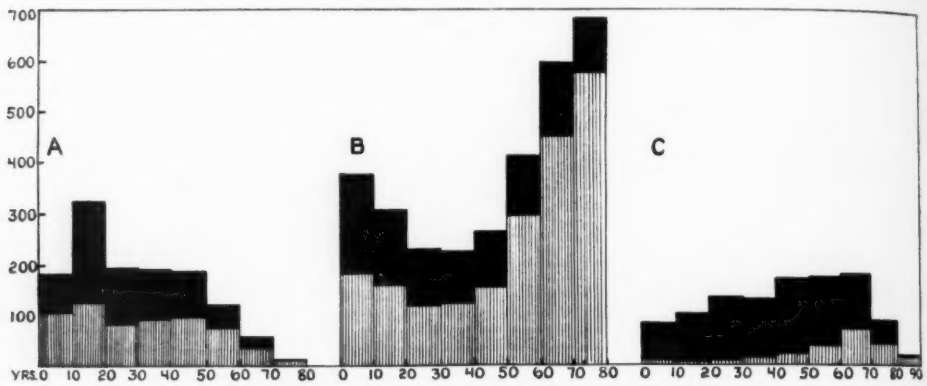


Chart 3.—Age incidence of and mortality from encephalitis in epidemics. *A*, in 1,272 cases of epidemic encephalitis (Parsons); *B*, in 3,118 cases in the Japanese epidemic from 1927 to 1929; *C*, in 1,097 cases in the epidemic of 1933 in St. Louis.

themselves manifest clinically. One noted first varying degrees of constitutional reaction. In the Japanese epidemic, the disease sometimes lasted for a period as short as twelve hours or as long as one-half year; the average duration was two weeks. The same observations hold true for the St. Louis epidemic. Also, as in all virus infections, the relative vulnerability of various tissues varied greatly. One may consider the neurotropic action as indicated by the small incidence of encephalitis in cases of pertussis, measles and vaccinia. Primarily, one sees a toxic reaction to the acute infection, and the extent or degree depends on the virulence of the infection and on the constitutional reaction of the patient. The neurotropic reaction varies greatly, but a fairly definite clinical entity is presented.

The early signs of invasion in the cases of encephalitis in St. Louis were not particularly impressive, except in younger persons, who may

have had acute gastro-intestinal upsets and convulsions. The prodromal symptoms were insidious. There was a period of from two to four days of general malaise and headache which became increasingly severe. The headache was usually frontal or parietal and frequently became so acute and severe that the patient was unable to move about, as either active or passive motion increased the pain. In such instances, stiffness of the neck and of the lower cervical and upper dorsal parts of the spine, as well as a Kernig sign, could shortly be observed. In a large proportion of patients, rheumatoid and myalgic pains throughout the body, but especially in the back and calves, were experienced in the early stages. Abdominal pain, with consequent nausea and vomiting, was not infrequent, especially in younger persons. Diarrhea occurred

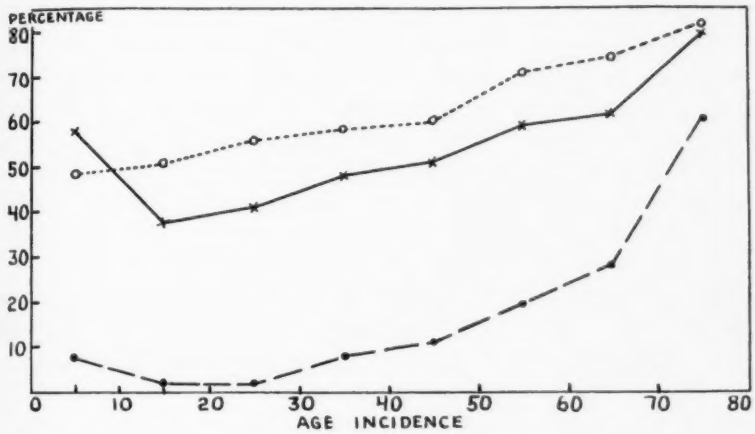


Chart 4.—Mortality rates according to age incidence in various types of encephalitis. The dash line indicates the mortality rate in the St. Louis encephalitis; the solid line, the rate for typical epidemic encephalitis; the dotted line, the rate for Japanese encephalitis from 1927 to 1929. The average mortality rate for the St. Louis encephalitis is 20.1 per cent; for epidemic encephalitis, 48.35 per cent, and for Japanese encephalitis, 66.96 per cent.

infrequently; constipation, frequently. Another symptom was sore throat. Suddenly, on from the second to the fifth day, a febrile reaction set in with an acute exacerbation of the headache. The pulse rate increased in proportion to the temperature, which ranged between 101 and 103 F. About one third of the patients showed bradycardia; only occasionally was tachycardia observed. Coarse regular tremors of the tongue and outstretched fingers appeared. The white blood cell count varied; the average for 198 cases was 15,400.

Some attention should be given to the complaint of sore throat. Despite the fact that it was not a constant symptom, physical examination showed dryness and redness of the throat and tongue. In such

instances, when the tongue was not furred and covered with detritus, it was smooth and "beefy" in appearance, and the fungiform papillae along the edge seemed to be distinctly enlarged. The redness of the mucous membranes was sometimes sharply limited by the anterior fauces. Often the tonsils were inflamed and the pharynx red. Whether this is characteristic of a virus infection or was due to dehydration is a debated question.

On from the fourth to the seventh day the headache was sometimes so severe that meningeal irritation was suspected. Lumbar puncture revealed that the spinal fluid was under increased pressure; the globulin was rarely increased; the sugar content and the colloidal gold curve were normal; cell counts in 279 cases averaged 116 cells, chiefly lymphocytes.

At this stage neurologic examination was of primary interest. The rigidity of the neck and Kernig sign were not always strikingly evident. This was especially difficult to evaluate in older patients with pathologic changes of the joints; one could, however, observe rigidity of the dorsal portion of the spine on having such a patient sit up. The headache, which in some instances was severe, in the milder cases usually abated after lumbar puncture. The tremors, which were coarse, were regularly elicited by voluntary motion. The pupils were usually smaller than normal, reacting well to light and in accommodation. Patients occasionally complained of photophobia, blurring and double vision, which could not be demonstrated clinically. Nystagmus was occasionally noted. Optic neuritis was reported but was not seen in the series of cases studied. Exophthalmos was also seen in a few cases. Occasionally, palsies of the face and tongue were seen. Involvement of the cranial nerves at this stage of the illness was of an irritative nature and transient. Later, when organic lesions occurred, such involvement was more striking, but nevertheless infrequent. Difficulty in speech was sometimes noted; whether it was due to tremor of the peripheral mechanism of speech, to the thick, poor articulation that occurs in toxic patients or to medullary lesions is difficult to determine. The last mentioned possibility is least likely, as the disturbance usually disappeared. The deep reflexes either showed no alteration or were slightly exaggerated in the irritative phase of the illness. There was a tendency for the abdominal reflexes to disappear. Signs of involvement of the pyramidal tracts were not conspicuous, but did occur.

Psychic disturbances were apt to appear as early as the third to the fifth day. Apprehension, confusion, restlessness, insomnia, delirium and stupor at times followed in rapid succession. The clinical picture was that of toxemia and prostration. The picture in mild or moderately severe cases should be differentiated from that of typical epidemic encephalitis. In the type of encephalitis under consideration, the patient

could usually be aroused and could cooperate in a confused, incoordinate way, but if his attention was not actively kept stimulated he resumed sleep. The sleep was not peaceful; motor restlessness was apparent. In epidemic encephalitis sleep is quiet and peaceful. The patient seems more comfortable and not particularly ill during the somnolent phase of the illness.

In the severe and fulminating cases the stupor was often deeper. An analysis of the 68 fatal cases at the City Isolation Hospital is shown in the following tabulation.

	Incidence	Percentage
Positive urinary findings	36	52.9
Pathologic reflexes	31	45.6
Suppression of deep reflexes	28	41.2
Coma or stupor	28	41.2
Bronchopneumonia	26	38.2
Defects of cranial nerves	16	23.5
Vesical incontinence	13	18.8
Bradycardia	20	29.4
Tachycardia	4	5.8
Shift of Schilling count to the left	30	
Cerebrospinal fluid cell count: 118 cells; highest 512, lowest 0 (116 cells average for 279 cases)		
White blood cell count: 12,470 cells; highest 22,000, lowest 1,300 (15,400 cells average for 198 cases)		

Patients with renal damage or bronchopneumonia had a poorer prognosis. The striking feature is that the spinal fluid count and the white blood cell count were not higher. The shift of the Schilling count to the left was merely indicative of an active infection and was not specific. The temperature was usually not high. Coma or stupor was undoubtedly underestimated, as well as urinary incontinence. In a large proportion of the cases, but by no means in the majority, pathologic toe signs were observed, and a suppression of reflexes was not uncommon. It was difficult to discern signs of a grave prognosis. The depth of the stupor and the critical appearance of the patient were the best criteria. Examination in such cases revealed pathologic lesions in the brain, lungs and kidneys, regardless of age.

The longer the period of delirium and coma, the more likely was one to find further neurologic manifestations. With the disappearance of the abdominal reflexes there was usually found some disturbance of the vesical and rectal sphincters. Constipation was such a frequent manifestation that no special note was made of it in clinical records. The vesical disturbance was of two varieties. Retention requiring catheterization was extremely frequent. Incontinence was infrequent and was a late development, although Kaneko and Aoki found that of 115 patients with Japanese encephalitis 40 per cent showed incontinence

and only 13 per cent retention. However, it is of interest that when the abdominal reflexes returned sphincter tone also returned.

In chronic cases one also observed palsies of the sixth, seventh and twelfth cranial nerves. Speech was absent in two patients throughout the course of illness despite the fact that the temperature soon returned to normal. Signs of involvement of the pyramidal tracts were found, and of the Chaddock, Babinski, Gordon, and Oppenheim signs, the Babinski sign seemed most constant. In patients who had been afebrile, well sustained ankle clonus without further signs of involvement of the pyramidal tracts persisted for months.

Chronic delirium was seen not infrequently in this group of cases and lasted for from several weeks to as long as three months.

Much interest centers about the question of residuals. Since the clinical course of the encephalitis observed in St. Louis shows more similarity to the Japanese type than to any other, a comparison of the two is of interest. The following symptoms have been noted after Japanese encephalitis:

Neurasthenic reaction (most common)
Headache
Insomnia
Excitability
Difficulty of concentration
Neuralgic pains throughout the body
Psychic and intellectual defects in children
Paresis and contractures
Poor coordination
Epileptiform attacks in children

In Kagawa, Japan, the center of the epidemic of 1924, about 2,000 cases occurred. In 35, or 1.7 per cent, the following residuals were observed:

	Number of Cases	Incidence Percentage
Paralysis	7	20.0
Disturbance of memory	6	17.1
Psychic disturbance	5	14.3
Defects of hearing	4	11.4
Headache	3	8.6
Dizziness	2	5.7
Disturbance of speech	2	5.7
Spasms of the extremities	2	5.7
Contractures of the leg	1	2.9
General tremor	1	2.9

While no true residuals had yet been observed, an examination made in December 1933 of approximately one third of the 1,097 patients afflicted in the St. Louis epidemic showed the symptoms and findings listed in table 3.

One must consider that many patients who have not reported are probably well. Also patients who were not well when discharged from the hospital are improving steadily, as more recent examinations have shown. Hence, one cannot speak of residuals in the same sense as in cases of typical epidemic encephalitis, but a further follow-up is necessary to confirm this impression.

TABLE 3.—*Disabilities from St. Louis Encephalitis in About One-Third of the 1,097 Cases Seen from Three to Five Months Later* *

	Incidence
General Disabilities	
Headaches	100
Insomnia	86
Drowsiness, lethargy	22
Nervousness	69
Weakness	24
Fatigability	24
Vertigo	56
Change in personality; irritability, excitability, moodiness	45
Difficulty of concentration	13
More Specific Disabilities	
Neuralgic pains	90
Tremors	72
Visual disturbance	66
Confusion, forgetfulness	54
Disturbance of speech	24
Paralysis	21
Difficulty of hearing	14
Ptosis of the eyelids	3
Epileptiform attacks	3
Problems of behavior in children	2
Chronic delirium	1

* Vital statistics from the Health Division of St. Louis, obtained through the courtesy of Elizabeth Breese, vital statistician.

REPORT OF CASES

The case histories of several patients seen at the City Isolation Hospital of St. Louis are presented because of the following interesting clinical features:

Exophthalmos, tremors, delirium and hyperkinesis.

Chronic delirium; later, signs of involvement of the pyramidal tracts and urinary incontinence.

Possible late toxic lesion; Bell's palsy bilaterally.

Mild attack with recovery and development of sciatic neuritis several months later.

Chronic delirium with complete amnesia for the illness, vesical disturbance, late defects of the cranial nerves, signs of involvement of the pyramidal tracts and marked tremors.

Tantrum-like, hyperkinetic behavior, posture akin to decerebrate rigidity, defects of the cranial nerves and absence of speech.

Acute meningeal irritation with jacksonian convulsions, defects of the cranial nerves and hemiplegia of long duration but showing gradual improvement.

Acute fulminating illness with marked prostration, development of bronchopneumonia and death in six days in a man of 48.

Less severe onset in a man of 72 with marked systemic reaction and death in eight days.

CASE 3.—P. R., a man aged 44, was admitted to the hospital on Aug. 30, 1933. On August 26 he had fever and malaise and on the following day he became confused and irrational. On admission, he seemed overactive, restless and boisterous and had to be restrained. He talked in a peculiar jerky, staccato fashion. His tongue showed a marked tremor. The throat and soft palate had a blotchy appearance, and the tonsils were very red. There were some rigidity of the neck and a Kernig sign. There was a coarse, regular tremor of the tongue. The eyes showed a slight icteric tinge in the conjunctivae, and there was some widening of the palpebral fissure, suggesting a mild exophthalmos, which had not been present before the illness. A blood count on August 28 showed 20,000 white cells. The spinal fluid contained 58 lymphocytes. The fluid obtained at another lumbar puncture on August 31 showed 31 cells, with 23 lymphocytes and 8 polymorphonuclears. The temperature on admission was 104.4 F.; it fell to 100 F. in four days by lysis and gradually became normal. Difficulty of speech persisted for some time, as did the tremor. The exophthalmos also persisted. However, the patient was improving steadily at the time of discharge on September 17.

Comment.—This case was of particular interest because of a disturbance of speech, which was partly accounted for by the coarse, regular tremors of the tongue and the delirious, hyperkinetic state, but also suggested a spastic defect of speech. There was also exophthalmos which first appeared during the illness. A neurologic examination did not reveal any other defects of the cranial nerves or any alteration in the reflexes.

CASE 4.—L. T., a married man, aged 34, was admitted to the hospital on Sept. 21, 1933, with a history of severe headache, fever, pains throughout the body, nuchal stiffness, restlessness, drowsiness and inability to void. The onset was on September 15. An examination of the spinal fluid on September 17 showed 184 lymphocytes per cubic millimeter. On examination the patient appeared somewhat drowsy. There was injection of the conjunctivae. The tongue and throat were red and dry. There were slight rigidity of the neck and a positive Kernig sign. The abdominal reflexes were absent. There were marked tremors of the lips, tongue and fingers. Because of the patient's inability to void, a retention catheter was used at first. On September 22 a lumbar puncture yielded fluid which had a count of 133 cells, with 90 per cent lymphocytes. The white blood cell count was 17,200, with 32 per cent lymphocytes and 62 per cent polymorphonuclears. The patient had a low grade fever, the temperature ranging from 100.4 to 97.8 F., throughout the illness. He was delirious during the entire six weeks of his stay in the hospital. He had urinary incontinence. At one time he complained of diplopia, although the neurologic examination revealed no defects in the cranial nerves. The abdominal reflexes failed to return and, although no pathologic signs were found in the toes, he suddenly showed bilateral ankle clonus, which was more marked on the right than on the left. This persisted at discharge on November 9.

When reexamined on December 16, the patient said that he had been confused, delirious and dizzy for about one week after discharge and that he seemed to forget easily. A neurologic examination showed some spasticity of the middle, ring and little fingers of the right hand. He also complained of impotence. He has, however, made a remarkable recovery.

Comment.—This case is of interest because of a chronic delirium, suggesting Korsakoff's syndrome, which lasted for about two months. There was urinary retention at first, and later an overflow phenomenon occurred. The abdominal reflexes were absent throughout the entire period. Also late in the illness there was evidence of involvement of the pyramidal tracts, and since the ankle clonus was more pronounced on the right the stiffness of the fingers of the right hand may be associated.

CASE 5.—J. A., a man aged 50, was admitted to the hospital on Sept. 10, 1933. He had had a cold followed by malaise two weeks before; three days previous to admission there developed severe headaches and pains in the legs. On September 9 he lapsed into stupor. On admission he was stuporous but responded to attention in a confused way. The pharynx was injected, and the tongue was dry. There was a marked rigidity of the neck. The deep reflexes were increased in the upper and decreased in the lower extremities. The abdominal reflexes were present. There was a tremor of the tongue. The white blood cell count was 16,200, with 72 per cent polymorphonuclears and 24 per cent lymphocytes. The spinal fluid showed increased pressure, a negative reaction for globulin, a positive reaction for sugar and 156 cells—106 lymphocytes and 50 polymorphonuclears—per cubic millimeter. The temperature on admission was 103 F.; it fell to 100 F. on September 21 and remained normal until discharge. During convalescence Bell's palsy developed, first on the left and two days later on the right side, and had not cleared up at discharge on October 8. Reexamination on December 9 showed some residual of the Bell's palsy on the left side, diminished hearing on the left side and a "drawing" sensation in the left leg, with fatigability on walking. There was also a slight impairment of memory.

Comment.—The development of peripheral facial paralysis during convalescence from the illness was an unusual toxic reaction. Impairment of hearing and memory were also noted.

CASE 6.—J. J. S., a man, aged 66, was transferred from another hospital on Aug. 31, 1933. On August 22 he had complained of severe occipital headache, fever, general malaise and pain in the neck. There was also slight vertigo. Examination at the first hospital showed pain and tenderness of the muscles of the neck on active or passive motion of the head. The pupils were small but reacted to light and in accommodation. The conjunctivae were injected. There was a questionable facial paresis on the right side. The knee jerks were greatly exaggerated; all the other deep reflexes were diminished. There was a tremor of the fingers. The Kernig sign was present. An examination of the spinal fluid on admission showed a normal pressure, a negative reaction to the Pandy test and 5 lymphocytes. On the following day bloody fluid was obtained. On August 24 the spinal fluid showed a positive reaction to the Pandy test (two plus), sugar, 85 mg. per hundred cubic centimeters, 66 lymphocytes and 8 crenated red cells.

The possibility of typhoid was considered. A blood culture was negative, and one of three stool cultures was positive. An agglutination test was positive for Bacillus typhosus in a dilution of 1:1,280. No physical signs of typhoid were found. When the patient was transferred he was afebrile. His only complaint was photophobia. The reason for further hospitalization was that he might be a carrier of typhoid. An examination on August 31 showed that the throat and

tonsils were injected and red. The spinal fluid contained 6 lymphocytes. He was discharged on September 14 after cultures of stools had been repeatedly negative. On December 12 he was reexamined. He complained of jerking of the legs and of some impairment of hearing in the left ear. The legs became progressively weaker; the ankle jerks were greatly diminished, and the pains suffered were indicative of sciatic neuritis, especially on the left side. An examination of the spinal fluid at this time gave negative results. The condition responded to treatment with diathermy and salicylates, but the disability at the time of writing is so great as to necessitate hospital care.

Comment.—The development of neuritis three months after encephalitis is unusual. Myalgic pains have been observed more frequently. While typhoid was suspected, it has been fairly definitely ruled out.

CASE 7.—M. M., a woman aged 47, entered the hospital on Sept. 13, 1933, with the complaint that she had suffered from headaches for the past two months; on September 10 she had severe pain in the back of the neck and head, fever and increasing drowsiness. She was very tremulous and delirious. On examination she spoke in inarticulate fashion, and the content was incoherent. The pupils were small but reacted to light and in accommodation. The conjunctivae were injected. There were coarse tremors of the tongue, lips and outstretched fingers. All the deep reflexes were hyperactive and equal, and there were no signs of involvement of the pyramidal tracts. The abdominal reflexes were absent. The neck was stiff, and the Kernig sign was positive. The white blood cell count was 5,400, with 24 per cent lymphocytes and 67 per cent polymorphonuclears. The spinal fluid was under increased pressure; the reaction for globulin was negative; the sugar content was 40 mg. per hundred cubic centimeters; the cell count was 178, with 98 lymphocytes. The patient rapidly went into coma and was fed through a tube and catheterized. On September 22 she became conscious; the neurologic examination showed a palsy of the lateral rectus muscle on the left side (she was said to have had an external squint from birth); there was facial weakness on the left, and the tongue protruded to the left. On October 4 she again became unconscious and showed extreme restlessness and nocturnal disorientation. At that time the spinal fluid contained 10 lymphocytes. There was a Babinski sign on the right, and since then there has been a well sustained ankle clonus on the right without further signs of involvement of the pyramidal tracts.

An examination on March 19, 1934, showed marked digital and oral tremors, hyperactive reflexes, an absence of abdominal reflexes and bilateral clonus, more marked on the right. The patient complained of headache, insomnia, restlessness, difficulty in memory and fatigability. She had no recollection of the entire stay in the hospital.

Comment.—This patient showed intermittent coma of long duration, urinary retention, involvement of the sixth, seventh and twelfth cranial nerves, late development of signs of involvement of the pyramidal tracts on the right, which persist, and complete amnesia for the entire period of hospitalization.

CASE 8.—O. D., a woman aged 22, single, entered the hospital on Sept. 27, 1933; she was transferred from another hospital because of her constant screaming and noisiness. When first hospitalized on September 12, she stated that she had had

severe frontal headache for three days, fever for two days and had vomited. An examination at that time showed transient periods of spasticity of all the extremities and hyperactive reflexes. The white blood cell count was 15,500, with 20 per cent stab forms, 58 per cent segmented forms and 21 per cent lymphocytes. The spinal fluid showed globulin (3 plus), 93 mg. of sugar per hundred cubic centimeters and 115 cells per cubic millimeter, 89 of which were lymphocytes. She rapidly became noisy and restless; she screamed loudly, and appeared delirious. When first seen she periodically cried out, but when quiet she lay with the head turned to the left and the eyes turned back to the right, and there was no movement of the eyes on passive motion of the head. There was paresis of the left side of the face. The abdominal reflexes were absent. The arms were flexed at the elbows, and the hands at the wrists and the lower extremities were rigidly extended, suggesting the posture of decerebrate rigidity, but no postural reflexes were obtained. There was incontinence of urine. There was no rigidity of the neck, and the Kernig sign was not present. The tongue was coated and dry, and the cervical nodes in the posterior triangle were enlarged. An examination of the lungs revealed moist râles at the bases. A lumbar puncture yielded fluid that showed increased pressure, a negative reaction to the Pandy test, a trace of sugar and 25 lymphocytes. Coarse, regular tremors of the head began to appear. There was evidence of consolidation in the lower lobe of the right lung. The urine contained pus cells. The patient was extremely restless, noisy and unable to sleep, despite hypnotics. The temperature rose to 105 F. Mercurochrome was injected intravenously as the condition became critical, and bleeding from the rectum followed. Rosenow's streptococcus serum was given without apparent improvement. There was wrist drop on the left, and abscesses developed in the axillary glands, which were incised. All the lymph glands were enlarged but smooth. On October 25 the white blood cell count was 12,200, with 72 per cent segmented forms and 7 per cent lymphocytes. The spinal fluid contained 57 mg. of sugar per hundred cubic centimeters; the Pandy test was negative, and there were 18 lymphocytes per cubic millimeter. A blood culture on October 28 was sterile. The condition of the chest had improved, but the elevation of temperature persisted. After this, the patient was transferred to two other hospitals in succession, and while in the last she still showed the same mental state; she was easily excited and screamed when examined. The deep reflexes were all exaggerated. The abdominal reflexes were absent. There were no pathologic signs in the fingers or toes, despite the spasticity of the extremities. The fingers were flexed so tightly that they could not be extended passively. There were also marked tremors, chiefly on raising the head. Periods of cyanosis and tachycardia were present. During the entire illness the patient did not speak, but on discharge from the last hospital, on March 7, 1934, she was beginning to do so. She also had begun to sit up. Recent reports state that she is walking a little and that she shows periods of spontaneous lateral nystagmus.

Comment.—This patient was the most seriously ill of those who recovered. She had pneumonia, urinary infection, abscesses of the axillary glands and a multiplicity of neurologic findings without signs of involvement of the pyramidal tracts, suggesting a lesion of the brain stem. The abnormalities of behavior, namely, excitability, noisiness and insomnia, were unusual, as was the absence of speech. She is improving steadily.

Case 9.—M. J. M., a girl aged 3 years, was admitted on Sept. 22, 1933, with the history that she had had fever, a stiff neck, malaise and headache for three days and had vomited for two days. The illness began on September 20 with fever and malaise, and as the temperature rose there were generalized convulsions lasting for several minutes. The child was semiconscious. The blood showed a white cell count of 16,000, and the spinal fluid contained 170 cells and a trace of globulin. On admission to the hospital, the patient seemed very drowsy, cross and irritable and could not be aroused. The neck was rigid. There was a bilateral Kernig sign. The pupils were small, but reacted to light. The abdominal reflexes were absent, and there was a Babinski sign on each side, more marked on the right. The tonsils and the pharynx were injected. The differential white blood cell count showed 61 per cent segmented forms and 32 per cent lymphocytes. The examination of the spinal fluid showed increased pressure, negative reaction for globulin and sugar and 85 lymphocytes per cubic millimeter. The child became stuporous on September 26, could not be aroused and was fed through a tube. The examination of the spinal fluid showed 97 mg. of sugar per hundred cubic centimeters, a trace of globulin and 151 cells, with 90 per cent lymphocytes. The legs showed marked rigidity; the pupils varied in size; the head was held turned to the right and drawn back. Convulsions which progressed from the right hand to the face, then to the right leg and later to the left side of the face began to occur. The convulsions increased and were difficult to control. Any movement would start them. The patient gradually improved. The rigidity of the neck became less marked. On October 5 otitis media developed on the left side, and the abscess was incised. The convulsions recurred. The cell count of the spinal fluid dropped to 79 on October 9 and to 54 on October 12. There were clonic movements of the left side of the body, and the patient was more rigid and stuporous and uttered a meningitic cry. An examination showed rigidity of the neck, a Kernig sign, hyperactive deep reflexes, absence of abdominal reflexes and a bilateral Babinski sign. On October 24 the knee jerks disappeared, but they returned on October 27. On November 2 the patient seemed more responsive and ate better. On November 9 she began to talk and showed a peculiar hyperkinetic activity when an attempt was made to examine her. She had a torsion movement, turning over and over when disturbed. She improved, but on discharge she had not recovered. She was seen on March 27, 1934. The mother stated that the patient had begun to walk only in the past month and had difficulty in using the right arm, which showed purposeless movements. An examination showed weakness and poor coordination of the right arm and leg. The right knee and ankle jerks were increased. The Babinski sign was positive on the right and questionable on the left. She dragged the right foot in walking.

Comment.—This patient's case is of interest because of the age incidence, the chronicity of the condition, its similarity to tuberculous meningitis, the marked signs of cerebral irritation and consequent jacksonian epileptic convulsions and the resultant hemiplegic picture. Despite the evidence of organic damage, the patient is showing steady improvement.

Case 10.—*History and Course.*—F. R., a man aged 48, entered the hospital on Aug. 21, 1933, having been transferred from another hospital. On August 18 he had severe frontal headache and fever. The temperature was 102.4 F.; the pulse rate, 84; the blood pressure, 135 systolic and 150 diastolic. The patient was lethargic and confused; his face was expressionless. The pupils were small. An examination of the fundi gave negative results. The tongue was dry. A neuro-

logic examination showed rigidity of the neck, a Kernig sign on the left, hyperactive deep reflexes, absence of abdominal reflexes and an unsustained ankle clonus on the left. There were no pathologic toe signs. The white blood cell count was 15,700, with 27 per cent stab forms, 48 per cent segmented forms and 19 per cent lymphocytes. Examination of the spinal fluid showed a positive reaction (two plus) to the Pandy test and 133 cells, mostly lymphocytes. There developed dulness and râles in the bases of the lungs. The temperature was 106 F. on admission and continued elevated until death on August 22. The pulse rate varied from 112 to 160.

Dr. H. McCordock gave the report of the autopsy.

Gross Postmortem Examination.—The body was that of a well developed, well nourished white man. Rigor mortis had not yet set in.

Brain: All the superficial blood vessels of the meninges were intensely congested. The larger veins were dark purple, but their smaller branches were bright red. These dilated vessels formed a red network that covered the brain. This vascular congestion was particularly prominent over the pons and brain stem. There were several irregular patches of hemorrhage about 1 inch (2.5 cm.) in diameter over the cerebral hemispheres, in the meshes of the subarachnoid space. The amount of cerebrospinal fluid did not appear to be increased. Section through the fresh brain showed all the blood vessels as red dots or streaks, depending on whether the vessel had been cut in cross-section or longitudinally. The entire gray matter of the cortex had a distinctly pink hue. A section through the pons revealed pink areas and in one or two places small punctate hemorrhagic areas about the size of a pinhead. Patches of pink tissue were also found in the basal ganglia and in the region of the substantia nigra.

Thorax: No fluid was present in either pleural cavity. The pericardium contained the usual amount of clear straw-colored fluid.

Heart: The heart was of normal size, and all the valves were delicate. On section, the muscle of the left ventricle was firm. There was very little sclerosis of the aorta.

Lungs: There was a marked hemorrhagic pneumonia involving both lungs. This process was especially well seen in the lower lobes posteriorly but was also present in the upper lobe of the left and in the middle lobe of the right lung. On section the pulmonary tissue was boggy, and when it was squeezed red fluid ran from the surface. This hemorrhagic and edematous consolidation resembled the lesions seen in the early stage of epidemic influenza. There was a calcified and caseous tracheobronchial lymph node at the root of the right lung, and a moderate number of calcified tubercles were observed on the pleural surface and in the substance of the lung.

Liver: The liver was of the usual size, had a smooth capsule and on section showed the normal lobulations. The central portions of the lobules were somewhat more congested than normal. The gallbladder contained green bile, and all the bile ducts were patent.

Spleen: The spleen was of moderate size and had a smooth capsule. On section, the pulp was dark purple, and the malpighian bodies were not very distinct.

Pancreas: The pancreas showed no unusual changes.

Stomach and Intestines: The gastric mucosa was smooth and velvety. No lesions were found in the intestinal tract.

Kidneys: The kidneys were about alike. The cortex and medulla were distinctly congested. There was a hemorrhagic pyelitis on each side. There were small punctate hemorrhages in the pelvic mucosa, and these extended down into the ureter for about one third of its length.

Bladder: There were a few petechial hemorrhages in the mucosa of the bladder.

Other Organs: The suprarenal glands, the genital organs and the thyroid gland appeared normal. There were small petechial hemorrhages in the submaxillary gland.

Microscopic Examination.—Heart: The cardiac muscle was normal. A large coronary artery showed moderate arteriosclerosis with fibrous thickening of the intima but no calcification.

Lungs: There was widespread bronchopneumonia. In many places the pneumonic exudate was of the usual purulent type, consisting of polymorphonuclear leukocytes, fibrin and red blood cells. In other areas the alveoli contained a coagulated pink, edematous fluid, in which were a few mononuclear cells. There were also many patches in which the alveolar walls were necrotic and the alveoli filled with blood. Hemorrhagic areas were also present in the walls of some of the smaller bronchi.

Liver: One large calcified, fibrous tubercle was present in the liver. Otherwise, no abnormalities were found.

Kidneys: All the blood vessels of the kidneys were intensely congested, and there were a few old cortical scars, with some fibrous glomeruli. Petechial hemorrhagic areas were present in the pelvic mucosa.

Other Organs: There were small areas of lymphocytic infiltration in the thyroid gland. Most of the acini were large and filled with colloid. Some of the acini, however, were very small and contained light-staining colloid. The spleen, pancreas and suprarenal glands showed no unusual changes.

Brain: Sections from various portions of the brain showed similar lesions. Everywhere the blood vessels were intensely congested. This was particularly true of those in the gray matter of the cortex, pons, medulla and spinal cord. Small hemorrhagic areas were present in the subarachnoid space where blood had leaked out from the distended vessels. In the substance of the brain, blood was often present in the perivascular lymph spaces, but no gross evidence of hemorrhages was found. There was a moderate amount of perivascular cuffing with lymphocytes. This lesion, however, was not as marked as those present in some of the other cases.

Small collections of cells were present in various situations; some of these were in the pons; others were in the cerebral cortex and in the spinal cord, especially in the gray matter. These cellular collections appeared to be groups of cells that had infiltrated foci of necrosis in the nerve tissue. Most of the cells were small round cells resembling lymphocytes. Others were large mononuclear cells, either of the glia type or large mononuclear phagocytes. Occasionally a small number of polymorphonuclear leukocytes were also present in these collections. When a nerve cell was found in one of these cellular collections it usually either was necrotic or showed signs of degeneration. Many nerve cells were shriveled and showed a dark-staining cytoplasm and a pyknotic nucleus. These shriveled dark-staining cells could be found side by side with perfectly staining cells. They were, therefore, not to be attributed to postmortem changes. In one section of the spinal cord the extensiveness of all the lesions described reminded one of the changes seen in anterior poliomyelitis.

Comment.—Clinically, this case did not differ from the usual moderately severe case. Bronchopneumonia developed, and the patient died.

CASE 11.—*History and Course.*—H. H. B., a man aged 72, who entered the hospital on Sept. 9, 1933, had not been feeling well and had had headaches for

the past week; on September 8, while at work, he felt drowsy and fainted. After this he had a sore throat and pain in the neck. The examination showed that the man was poorly nourished. The tongue was coated, and the throat was red. There were rigidity of the spine and a positive Kernig sign. There were coarse tremors of the tongue and fingers. All the deep reflexes were present and equal. The abdominal reflexes were absent. There were no pathologic toe signs. The white blood cell count was 12,800, with 72 per cent polymorphonuclears and 19 per cent lymphocytes. The examination of the spinal fluid showed 1,200 white cells and many crenated red cells. The patient had to be catheterized. He improved slightly after a lumbar puncture. Then hypostatic pneumonia developed. The temperature at the beginning of the illness was 105 F.; it fell gradually to 100 F. The pulse rate varied between 60 and 100. The patient died on September 16.

Autopsy.—Dr. H. McCordock gave a brief report. The brain was edematous and hemorrhagic. The vessels over the surface were dilated, and there was evidence that a large amount of hemorrhage had occurred in the subarachnoid region. The subdural area was filled with fluid. On section many dilated vessels were visible, with hemorrhagic areas throughout; these changes were most marked in the pons and medulla. There was a region of softening in the left motor area.

The endocardium of the heart and the walls of the aorta showed sclerotic areas. The vessels were somewhat sclerotic.

The lungs showed a mild hemorrhagic type of pneumonia, especially at the base of the right lung, with a large amount of sanguineous fluid which could be expressed on pressure.

The spleen was enlarged one and one-half times and was very soft and hemorrhagic.

The right kidney was somewhat enlarged. The capsule could be stripped fairly easily. The entire pelvis was mottled, infected and dark red. The glomeruli were distended and stood out. The left kidney was similar to the right, save for a large cyst. There was mild cystitis.

The microscopic examination of the brain showed a few lymphocytes and red blood cells in the meninges. There was vascular congestion in all the vessels of the brain, but no blood or hemorrhagic areas were obtained in the brain tissue. Many perivascular cuffs and glial nodules were seen, as well as patches of diffuse cellular infiltration and degeneration of ganglion cells. The lesions were distributed as follows: There were a few in the cerebrum, many in the basal nuclei, midbrain and pons and none in the cord or in the cornu ammonis. Some arteriosclerosis was present.

Infective material was recovered in two instances following the inoculation of animals with material from the brain.

Comment.—This is a typical fatal case. The age incidence and the symptoms—headache, sore throat, tremor, Kernig sign, stiff neck, absence of abdominal reflexes, delirium and bronchopneumonia—constitute the usual picture.

SUMMARY AND COMMENT

From a neurologic point of view the sequence of signs and symptoms in this type of encephalitis may be indicated as follows:

1. A prodromal period with lassitude, malaise, mild headache, occasional sore throat, gastro-intestinal upsets and fever.
2. Myalgic and neuralgic pains.

3. Headache—frontal, parietal and occipital—becoming acute.

4. Rigidity of the neck, immobility of the dorsal portion of the spine and a Kernig sign.

5. Increase of deep reflexes, or no alteration in the early stages, and subsequent suppression.

6. Moderately coarse tremors of the intention type in the fingers, lips and tongue.

7. Some reduction in the size of the pupils.

8. Absence of abdominal reflexes.

9. Delirium, coma and stupor due to toxemia.

10. Disturbances of the vesical and rectal sphincters with consequent retention and occasional incontinence and constipation.

11. Signs of involvement of the pyramidal tracts, transient and shifting at first, but more persistent when found later in the illness.

12. Involvement of the cranial nerves: early and infrequent blurring, diplopia, nystagmus, exophthalmos, facial palsy, deafness, vertigo and dysarthria; late and rare—palsy of the lateral rectus muscles, facial palsy, disturbance of speech and paresis of the tongue.

13. Late results: paresis and paralysis of the extremities and hemiplegias; myalgia and neuralgia; fatigue reactions; mental disturbances, such as irritability, disturbances of concentration and memory, confusion, as in Korsakoff's syndrome, and, in children, behavior problems, e. g., stealing and lying.

A statistical analysis of data compiled by Mr. Robert Drury on 300 patients seen at the City Isolation Hospital of St. Louis shows that about 65 per cent presented varying degrees of delirium or coma; 39 per cent, some sign of involvement of the pyramidal tracts; 11 per cent, involvement of the cranial nerves; 8 per cent, disturbance of speech, and 1.3 per cent, hemiplegia.

The diagnosis may present difficulty early in the disease and in mild cases. Conditions to be differentiated are: tuberculous meningitis, other forms of encephalitis due to infections with virus, syphilitic meningitis, cerebral hemorrhage, malaria, typhoid and endogenous and exogenous intoxications.

Clinically, cases may be classified as: (1) abortive—with such mild symptoms that they are undiagnosed; (2) mild—probably showing only the first eight findings indicated in this schema; (3) severe—such as cases 1 and 2, and (4) very severe and fulminating—such as cases 4, 7, 8, 9, 10, and 11.

Kaneko and Aoki [1] in discussing Japanese encephalitis classified it according to the course and intensiy of the illness, the portions of the central nervous system most involved—that is, the localization of the pathologic changes—and the mental state. The mental state is of some significance. The patient, according to these authors, is: (1) comatose;

1. Kaneko, K., and Aoki, Y.: Ueber die Encephalitis epidemica in Japan, Ergebn. d. inn. Med. u. Kinderh. **34**:342, 1928.

(2) delirious—hyperkinetic; (3) apoplectic—hemiplegic; (4) somnolent—lethargic (seldom), or (5) subject to choreiform movements. In a large number of cases in the St. Louis epidemic the mental state can be classified under one of the first three subdivisions. The toxic delirious reaction is characteristic for this epidemic.

Therapy has not been discussed. Most patients obtained marked and progressive relief from the first lumbar puncture. If indicated, puncture was done repeatedly. Forcing fluids, the avoidance of vesical complications and frequent enemas are also necessary. Rosenow's streptococcus serum and intravenous injections of mercurochrome and metaphen do not seem to help. Other treatment is symptomatic. The question of obtaining protection with convalescent serum will arise. Since the incidence per hundred thousand of the population was 104.7 and the death rate 21, the wisdom of such a procedure is questioned.

The question of recurrence of the type of encephalitis observed in St. Louis is often discussed. Encephalitis B—found in Japan—occurred in 1871, 1873, 1901, 1903, 1909, 1912, 1916 and 1919. No statistics, however, are available for the period before 1924. For these years since this time, the following data are available:

Year	Number of Cases	Percentage of Mortality
1924	6,949	59.9
1925	49	59.2
1926	1,766	38.9
1927	953	70.0
1928	70	71.0
1929	2,058	65.0

As in other virus infections, such as poliomyelitis, and as suggested from the statistics in the tabulation, it is impossible to predict the future occurrence. Since serum from patients who had encephalitis B does not protect animals inoculated with the virus of the St. Louis type, it is known that the viruses are different. The factors predisposing to an outbreak of any virus infection are unknown.

THE PYKNOLEPSIES

SMITH ELY JELLIFFE, M.D.
AND
J. NOTKIN, M.D.
NEW YORK

Among the paroxysmal disorders is a symptom complex occurring in childhood and sometimes in adolescence to which Friedmann drew attention in 1906. The syndrome consists of peculiar attacks, often very frequent, one hundred or more sometimes occurring in a day, and lasting only a fraction of a minute. Friedmann spoke of a short, partial interruption in the thinking and speaking processes and in the voluntary movements. According to him the psyche is in a state of suspension, but there is no real loss of consciousness and no involvement of the mechanism of coordination, even though at times the innervation that regulates the capacity to stand is implicated. He also observed a turning upward of the eyeballs, a blinking of the eyelids and a relaxation of the extremities, though not to the point of a complete loss of muscular tonus.

Friedmann's original publication aroused considerable interest in this syndrome, which he regarded as rare, and a number of publications have appeared since. It must be added, however, that Friedmann himself admitted that the phenomenon had been described previously by older observers. As we had an opportunity to study the condition, we decided to review the cases recorded in the literature, to report our own observations and to discuss the nature and the etiologic possibilities of the pyknoleptic attacks.

NOMENCLATURE

Friedmann [1] had difficulty in choosing a suitable name for the set of symptoms he described, and as he thought at first that he was dealing with narcoleptic attacks, he spoke of *die kurzen narkoleptischen Anfälle*—short narcoleptic attacks. He did not believe originally that these attacks were epileptic seizures, and consequently he also spoke of *die nicht epileptischen Absencen*—nonepileptic absences. Heilbronner [2] in the same year reported a number of cases and offered the descriptive

---

Read by title at the Sixtieth Annual Meeting of the American Neurological Association, Atlantic City, N. J., June 6, 1934.

1. Friedmann, M.: Ueber die nicht-epileptischen Absencen oder kurzen narkoleptischen Anfälle, Deutsche Ztschr. f. Nervenh. **30**:462, 1906.

2. Heilbronner, R.: Ueber kleine Anfälle, Deutsche Ztschr. f. Nervenh. **31**: 472, 1906.

name of *gehäufte kleine Anfälle der Kinder*—multiple small attacks in children. Sauer [3] in 1912 introduced the term "pyknolepsy," considering the extremely short duration of the attacks. This term was promptly accepted and has been used by all the other authors since. However, Gruhle,[4] in his review in 1924, referred to these attacks as type 1 (Friedmann) and to the so-called Gélineau [5] attacks as type 2. Henneberg [6] also distinguished the former type of attacks from Gélineau's narcolepsies and proposed that they be called "ekleptic" or "ekleiptic." These terms, however, were not favored by Redlich.[7] As a rule, the attacks are now universally described under Sauer's designation, "pyknolepsy."

SYMPTOMATOLOGY

We have already indicated the main features of the symptom complex as described by Friedmann.[1] We may add that, according to him, the physical and the intellectual development of the child do not suffer. The condition may last for a few years and disappear about the time of puberty. On looking over the reports of cases in the literature, however, we have noted that a number of authors have reported under the name pyknolepsy a variety of conditions which do not fit into the original picture given by Friedmann. In many cases frank epileptic attacks were described and were called pyknoleptic solely because of their frequency or their occurrence in children. We have, therefore, reviewed all the cases reported in the literature, beginning with those of Friedmann, and the tabulation of the casuistic material resulted in five groups. The first group comprises cases in which there were numerous attacks of sudden staring, with blinking and immobility, lasting only one or two seconds, without apparent impairment of consciousness. The second group includes cases in which amnesia, rigidity of the pupils and occasional sphincteric relaxation during attacks were noted. The third group comprises cases in which in addition to the symptoms described there were involuntary movements in the form of twitchings in the various groups of muscles. The fourth group consists of cases with a history of pyknoleptic attacks which later evolved into generalized convulsions. Finally, in the fifth group we have assembled cases of unquestionable classic epileptic seizures.

3. Sauer, H.: Ueber gehäufte kleine Anfälle bei Kindern (Pyknolepsie), Monatschr. f. Psychiat. u. Neurol. **40**:27, 1912.

4. Gruhle, H. W.: Ueber die Fortschritte in der Erkenntnis der Epilepsie in den Jahren 1910-1920 und über das Wesen dieser Krankheit, Zentralbl. f. d. ges. Neurol. u. Psychiat. **34**:1, 1924.

5. Gélineau: De la narcolepsie, Gaz. d. hôp. **53**:626, 1880.

6. Henneberg, R.: Ueber genuine Narkolepsie, Neurol. Centralbl. **35**:282, 1916.

7. Redlich, E.: Ueber Narkolepsie, Ztschr. f. d. ges. Neurol. u. Psychiat. **95**: 256, 1925.

We have collected altogether 190 cases reported up to 1931. One hundred and six of these cases can be called pyknoleptic, and the other 84 made up the fifth group of cases, those of generalized attacks. Sixty-seven of the 106 cases were in girls and 35 in boys, while the remaining 4 were described as occurring in "children" without indication as to the sex. The age at the onset of the attacks ranged between 4 and 12 years. In 11 cases there was a definite history of epileptic heredity. In 33 the heredity was "positive," including various types of psychoses, psychopathy, organic disease of the brain or alcoholism. In 26 cases the heredity as reported was "negative," and in the remainder of the group no mention of hereditary taints was made.

Before considering the etiologic and pathogenic possibilities we shall report our own observations.

REPORT OF CASES

CASE 1.—*One generalized convulsion at the age of 3. Since the age of 7, pyknoleptic attacks with gradual intellectual impairment. Decrease in the number of seizures under therapy with phenobarbital.*

History.—A Jewish girl, aged 11 years, born in the United States, the oldest of four children, weighed 8 pounds (3,628.73 Gm.) at birth. She had her first teeth at the age of 1 year, and the fontanels closed at the age of 2. She walked and talked at 2 years. When she was 3, she suddenly fell, losing consciousness, and remained on the ground for five minutes. Her face became blue, but there were no twitchings or urinary emission. She recovered entirely after this attack. The following year she had measles and whooping cough. She started going to school at the age of 5 and reached grade 4 A at 11. After the child was 7 years of age the teachers and the parents noted that at times she suddenly became "dreamy" and appeared to be "unconscious" for a few seconds. She did not fall during these attacks. She usually recovered completely and continued her interrupted activities. The mother stated that during a fit she looked "dopey"; her head trembled, and she stood still for about a second. The attacks occurred at any time of the day and even while she walked in the street. While at play with other children she sometimes suddenly stopped; her eyelids began to blink, and she mumbled something to herself. Attacks occurred while she was eating, and she dropped whatever she had in her hand. Occasionally she closed her eyes during the seizures, but as a rule the eyes remained wide open. At first the attacks occurred from three to four times a day, but from the age of 10 to 11 they took place almost hourly. She had been bright and intelligent until the onset of this condition, but subsequently her progress in school, particularly in arithmetic, became poor. She also became irritable and nervous, and she frequently quarreled with her younger brother. She came to the New York Post-Graduate Medical School and Hospital, accompanied by her mother, on April 22, 1930.

Examination.—The child had a rather overdeveloped adiposity, without neurologic signs. The blood count revealed: red cells, 4,850,000; hemoglobin, 85 per cent; white cells, 5,750; polymorphonuclear neutrophils, 67 per cent; eosinophils, 1 per cent; basophils, 1 per cent; mononuclears, 1 per cent; small lymphocytes, 11 per cent, and large lymphocytes, 19 per cent. The Wassermann and Kahn precipitation tests of the blood were negative. The blood chemistry was normal,

showing: uric acid, 4.2 mg. per hundred cubic centimeters; urea nitrogen, 10.7 mg.; sugar, 0.098 Gm., and chlorides, 0.529 Gm. The basal metabolic rate was 3 per cent below normal. The intelligence quotient was that of a moron.

Course.—The patient had fewer attacks under medication with phenobarbital during the three months she was under observation. Then the family moved away, and their whereabouts is unknown.

CASE 2.—*Pyknoleptic attacks with amnesia and static pupils during the seizures. Improvement under therapy with bromide.*

History.—A boy, aged 8 years, born in the United States of healthy parents, the youngest of three siblings, began to walk at the age of 13 months and to talk at the age of 2 years. He had chickenpox at 5. At this age he began going to school, reaching grade 3 B at 8. He was entirely well until Sept. 19, 1929, when he was 7 years of age; then he began to have short attacks during which he remained still for a while. During these attacks he did not answer when spoken to and occasionally pulled at his trousers or stockings. At times he had blinking of the eyelids. These "spells" occurred while he was playing, riding his bicycle or walking. When riding or walking he slowed down his bicycle or his step. Occasionally the child seemed to know what was going on during attacks, as he complained that his vision was temporarily blurred. At other times he imagined that he was playing in school. He also had attacks while he was eating, and on these occasions he continued to masticate. He came with his mother to the neurologic clinic of the New York Post-Graduate Medical School and Hospital on April 1, 1930.

Examination.—The child, of a gracile habitus, weighed 58½ pounds (26.5 Kg.) and was 4 feet and 8 inches (142.24 cm.) tall. The neurologic status and the eyegrounds were normal. However, the patient did not cooperate for the various laboratory tests, except that he permitted a roentgenogram of his skull to be taken; this revealed a sella turcica about 40 per cent undersized with bridging of the clinoid processes. The intelligence tests showed his mental age to be 11 years; he was very shy and averse to expressing himself verbally. His planning ability was that of a child aged 10½.

Course.—On two occasions he was seen by one of us during an attack. At the onset of the first attack he suddenly became immobile and began to blink his eyelids. There were a few movements of the head similar to spasmus nutans. During the seizure the pupils were about 4.5 mm. in diameter and did not react to light. The attack lasted only a few seconds; when questioned afterward the child said that he had no knowledge of having had a seizure. He was seen in another attack a week later; this time he rolled his eyes, moved his lips and took deep inspirations. The attack lasted about five seconds; the pupils were dilated and did not react to light.

He responded fairly well to treatment with a preparation of bromide. A further follow-up was impossible as the patient could not be located.

CASE 3.—*Fracture of the skull at 4½ years. Generalized convulsions since the age of 8½. Pyknoleptic attacks since the age of 9. No response to antispasmodic therapy.*

History.—A boy, aged 9, born in the United States of Jewish parents, began to walk at 14 months and to talk at 2 years. He had measles at 2 and scarlet fever at 4. He began going to school at 6 and made poor progress. When 4½, he fell from a window 20 feet (6.09 meters) high. He sustained a fracture of the right temporoparietal bones and was unconscious for five days. He vomited on the way to the hospital. On the sixth day he opened his eyes and asked for ice-cream.

The next morning he recognized his mother. He was well at that time, and there was no evidence of paralysis. He remained in the hospital for three weeks, during which he was apparently in good condition. The wound of the scalp healed, and he was taken home. Since then his parents noted that he was rapidly gaining weight. The mother said that "he was swelling up." It was difficult to discover how long the gain in weight lasted, but the mother claimed that after a while he began to lose the excess weight. Since the accident he had slept poorly, and sometimes he sat up at night. On Nov. 22, 1926 (four years after the injury), the patient vomited three or four times. The following night he suddenly had a convulsion while he was asleep. The parents heard him moaning and found him stiffened; his pillows were wet. They woke him, but he did not seem to recognize them and closed his eyes immediately. A few minutes afterward he opened his eyes and began to speak normally.

The second attack occurred on December 15 at about 6 a. m., while he was asleep. A brother who was sleeping with him was awakened by his tossing around; he soon fell out of bed. The mother found him on the floor, "stiff," with the eyes closed; it took ten minutes to awaken him. He had a third seizure on December 22.

In 1927 he had one attack on each of the first three consecutive days of November, all in the daytime. During the third attack he was seen by the father; the head was turned to the left, and there were twitchings in the left arm.

He had another attack on Nov. 17, 1928, at 8 a. m., while he was asleep. There were twitchings in the left arm and in the left side of the face. Between that time and his admission to the clinic he had eight or nine similar attacks.

In 1927 the patient began to have, in addition, attacks which lasted only a few seconds. He did not fall, and he knew everything that was going on during the attacks; he felt twitchings in the left arm and in the left side of the face; he could not talk during the seizures, which occurred several times daily. One of us saw him during one of these attacks. The boy became suddenly immobile, standing rigidly; he turned pale, and the eyes were fixed and glary. By the time the examiner came near him he had recovered from the attack, and he told him that he knew what was going on all the while.

He was brought to the neurologic clinic of the New York Post-Graduate Medical School and Hospital on Dec. 20, 1930.

Examination.—The boy was stout, with a feminine body contour. The deep reflexes were exaggerated on the left; there were ankle clonus and fanning of the toes on the left; the left abdominal reflexes were absent, and the left cremaster reflex was weaker than the right. A slight systolic murmur was heard at the apex but was not transmitted. Roentgenologic examination revealed a somewhat rectangular defect in the middle of the right parietal bone, measuring about 2 inches (5 cm.) in length by ¾ inch (2 cm.) in diameter. The blood count revealed: red cells, 4,210,000; hemoglobin, 80 per cent; color index, 0.96; white cells, 8,800; polymorphonuclear neutrophils, 50 per cent; transitionals, 1 per cent; mononuclears, 2 per cent; small lymphocytes, 40 per cent, and large lymphocytes, 7 per cent. About one fifth of the red cells were microcytic. The Wassermann reactions of the blood and spinal fluid were negative. The basal metabolic rate was 17 per cent below normal. The sugar tolerance was low.

An intelligence test showed the patient's mental age to be 7 years and 2 months and his intelligence quotient to be 80—that is, dull intelligence. He appeared to be pleasant; he talked spontaneously and was en rapport with the examiner but was somewhat restless and fidgety; he showed some difficulty in attention.

Course.—The patient did not respond to treatment with phenobarbital or with bromide, and the parents refused to bring him to the clinic for further studies.

COMMENT

There is considerable controversy regarding the nature and the possible etiology of the pyknoleptic attacks. Some authors regard them as being related to narcolepsy, others to hysteria; a few investigators have expressed the belief that many cases show evidence of a spasmophilic diathesis. Views have also been expressed that the attacks are essentially epileptic and that they are organically conditioned. We shall, therefore, consider briefly these various approaches.

Relationship to Narcolepsy.—Friedmann [1] originally thought that he was dealing with narcoleptic attacks in children. He saw the following analogies: the frequency of the attacks, the supposed lack of response of certain patients to medicinal treatment and the apparent absence of mental deterioration. Such a postulation is rather impressionistic, especially since Friedmann drew his conclusions from a relatively small number of observations. The narcoleptic attacks are apparently attacks of sleep or of some condition resembling sleep. In addition, in the so-called true narcolepsy there are also cataleptic attacks with momentary loss of muscular tonus, usually produced by laughter or some other affect. The pyknoleptic attacks are not attacks of sleep; there is only a cessation of all activities with clearness of sensorium in many instances. The affective loss of tonus is not observed in these children. The patient may fall during an attack, but this is due to a disturbance in coordination as in general epilepsy.

Relationship to Hysteria.—Heilbronner,[2] in 1906, in reporting his cases under the descriptive name *gehäufte kleine Anfälle,* claimed that the attacks were hysterical. He based his theory on the observation that his patients were amenable to psychotherapy, especially to isolation therapy. Engelhard [8] and Bonhoeffer [9] agreed with Heilbronner [2] as to the hysterical nature of the attacks. Westphal [10] expressed sympathy with this view, emphasizing that in a number of the children that he had observed the attacks occurred shortly after an emotional upset. Children have been observed to have attacks, even with a fall, during class hours when they were suddenly called on to recite or to perform some task. Fright, for instance, seemed to have been the precipitating

8. Engelhard, C. F.: Gehäufte kleine Anfälle bei Kindern, Psychiat. en neurol. bl. **18**:197, 1914.

9. Bonhoeffer: Ein Fall von Narkolepsie, Berl. med. Wchnschr. **27**:1250, 1911.

10. Westphal, K.: Zur Psychogenese und Therapie pyknoleptischer Anfälle, Ztschr. f. d. ges. Neurol. u. Psychiat. **138**:745, 1932.

factor in the cases of Zappert,[11] and Stier [12] and in the first and fourth cases in Friedmann's [13] second series.

Of the cases in the literature, the eighth in the group of Sauer [8] and the first in the group of Ratner [14] present considerable psychologic material, and we shall, therefore, briefly refer to them here.

Sauer's Case 8.—A girl, aged 10 years, of healthy parentage and of normal development, had had whooping cough with bronchopneumonia and pleuritis at the age of 9. A few months after recovery, and following the death of a brother on the battle-field, there developed a severe fear reaction. She began to speak of Russian soldiers, saying frequently: "The Russians are coming." Shortly afterward she began to have attacks, at first on Saturday evenings only and later every day, during which she yelled, "The Russians are coming," and fell. The attacks lasted only a few seconds and occurred as often as twenty times a day. She recovered with a smile on her face. In bad weather, when she remained indoors, the attacks were more frequent. Sometimes, she ran around, threw herself on the floor and gasped for air, speaking in a fearful manner, as if something were taken from her. The attacks occurred under all kinds of circumstances. Sauer noted no changes in the personality, and the patient exhibited no abnormal physical signs.

Ratner's Case 1 (*from his first series*).—A girl, aged 18, of healthy parentage, had had the usual diseases of childhood and was well developed physically. Mentally she was normal until the age of 7 when she saw prisoners of war in her village. She became frightened, ran home and fell "unconscious" in the arms of her mother. After that she began to have short attacks which occurred while she was talking; she suddenly broke up a sentence, remained still for a second and then continued the interrupted conversation as if nothing had happened. She never fell, and there was no incontinence. In the beginning she had as many as one hundred and fifty attacks in a day, but later the average was forty a day. When she was overcome by an attack while on the street, she kept on "walking automatically" and avoided every hindrance in her way. Occasionally she had a feeling of being drowned, "similarly to death one lives through while asleep." On one occasion she had an attack while in a train. She heard the conductor calling the name of the station, left the train, took a wrong road and woke up three hours later, sitting in snow in a forest.

Physical examination revealed a pyknic habitus, with inequality of the palpebral fissures and anisocoria. There was a lively bilateral ulnar phenomenon; the right nasolabial line was somewhat ironed out. Biochemical laboratory tests gave negative results.

While the patient was in the hospital attacks were artificially produced by hyperventilation. During the menstrual periods she had thirty attacks in a day. During the night of Jan. 23, 1927, she woke up several times; she slept until noon

11. Zappert, J.: Zur Prognose der Epilepsie im Kindesalter, Med. Klin. **8**: 229, 1912.

12. Stier: Zur klinische Stellung und Prognose der gehäuften kleinen Anfälle der Kindern, Ztschr. f. d. ges. Neurol. u. Psychiat. **80**:143, 1922.

13. Friedmann, M.: Zur Kenntnis der nichtepileptischen Absencen im Kindesalter, Ztschr. f. d. ges. Neurol. u. Psychiat. **9**:245, 1912.

14. Ratner, J.: Beitrag zur Klinik und Pathogenese der Pyknolepsie, Monatschr. f. Psychiat. u. Neurol. **64**:264, 1927.

the following day. She intended to visit a friend, but instead began to wander around the town. She had a more or less correct memory of stations and other places and of conversations with strangers. People apparently noticed her condition, and somebody suggested that she go home. She refused to do so. When three men insulted her her mind became clearer for a while, and she threatened to call a policeman. After riding in street-cars for hours she began to ring doorbells; as she became hungry she asked a policeman for bread, but she could not tell him where she lived. She was taken to a police station where she was given some food. She ate hastily and greedily. She then accommodated herself on a few chairs and fell asleep. She woke up the next morning and felt refreshed. She explained to the police authorities the nature of her illness and was released.

There is little material in the cases reported in the literature which permits a glance into the submerged dynamic material. It is possible that, as in general epilepsy, there are borderline cases in which it is difficult to make a differentiation between so-called functional and organic fits. However, as in "affectepilepsy" [15] one may be dealing with explosive material which is readily ignited by any sort of spark, emotional or organic. Again, there may be a state of continuous conflict in the sphere of the instinctual drives, a state which in itself may lower the threshold of convulsibility.

Relationship to Spasmophilia.—In 1911 Mann [16] suggested an affiliation of the pyknoleptic attacks with the spasmophilic diathesis. Sedgwick [17] offered the same suggestion, emphasizing that in certain cases the Chvostek sign is present. This is a rather important observation, since galvanic irritability is generally increased after an epileptic attack, as has been shown especially by Foerster.[18] It is also interesting to note in this connection that Römer [19] found Erb's phenomenon in 40 of 251 epileptic patients. Bonhoeffer [9] and Klieneberger [20] could not confirm the theory of spasmophilic irritability suggested by Mann.[16] It is, however, important to mention that Aron [21] found electric hyperexcitability to be present in 25 per cent of children of school age and a Chvostek sign in 12 per cent. This may indicate, at least, that there

15. Notkin, J.: "Affectepilepsy" and "Hysteroepilepsy": A Study of Convulsive States in Psychopaths, J. Nerv. & Ment. Dis. **72**:135, 1930.

16. Mann, L.: Erregbarkeitssteigerung bei narkoleptischen Anfällen, Ztschr. f. Elektroth. **13**:82, 1911.

17. Sedgwick, J. P.: Spasmophilia with Special Reference to Familial Reactions and Repeated Absences, Am. J. Dis. Child. **7**:140 (Feb.) 1914.

18. Foerster, O.: Hyperventilationsepilepsie und Aussprache dazu, Jahresvers. d. Gesellsch. deutsch. Nervenärzte, 1925, p. 155.

19. Römer, K.: Das Erbsche Phänomen bei der Epilepsie, Ztschr. f. d. ges. Neurol. u. Psychiat. **84**:1, 1923.

20. Klieneberger, O.: Ueber Narkolepsie, Berl. klin. Wchnschr. **6**:246, 1913.

21. Aron, H.: Ueberregbarkeit im Kindesalter, ihre Bedeutung und Behandlung, Therap. d. Gegenw. **66**:158, 1925.

is greater excitability of the nervous system in children, which in certain cases may facilitate the occurrence of the pyknoleptic attacks.

Relationship to Epilepsy, Especially to Petit Mal Attacks.—Friedmann [1] did not believe originally that the attacks that he described in 1906 were related to epilepsy. His main reasons for not considering these attacks as epileptic were the apparent preservation of consciousness and the seeming absence of irritative phenomena. This reasoning is erroneous, since partial preservation of consciousness in so-called true epileptic attacks has been observed by Oppenheim,[22] Marchand,[23] and Engelhardt [8] and by us. However, Friedmann [24] admitted later, in 1915, that some of the pyknoleptic attacks observed by him might have been related to epilepsy. Many cases reported in the literature, including many of Friedmann's own cases, were undoubtedly of the usual epileptic type. In our tabulation of 190 cases we have eliminated 84 as frankly epileptic. The only apparent reasons that they were reported under the heading pyknolepsy were the frequency and the relative shortness of the seizures. We shall sketchily refer to some of the remaining 106 cases which have some of the features ordinarily seen in epileptic attacks in order to show that in most instances pyknolepsy is closely related to epilepsy.

Unconsciousness was definitely described in Heilbronner's [2] second and third cases; nocturnal attacks occurred in the sixth; the patient in the eighth case had, in addition to the pyknoleptic attacks, generalized convulsions at the age of 11 and later. In Friedmann's [13] second series (among these cases are a number from the first series), the patient in case 2 had nocturnal seizures, with fixed pupils during the attacks, while the patient in the third case usually fell asleep after attacks and once remained unconscious for an hour. Mann's [16] patient had generalized convulsions at 3½ years of age, and later tetany-like states with fixed pupils. The third of Engelhardt's [8] patients had opisthotonos; the seventh had epileptic attacks when 1½ years old; the twelfth had spasms and cyanosis in infancy; the fifteenth had nocturnal attacks with twitchings and later frank epileptic attacks in addition to the pyknoleptic seizures; the seventeenth occasionally became incontinent and had momentary losses of vision and hearing, and in addition had twitchings in the various groups of muscle. Sauer's [3] second patient had twitchings of the muscles of the hands and movements of the head and torso; the third, nocturnal attacks with incontinence; the fifth, occasional incontinence during attacks; the sixth, grinding of the teeth and somnolence after attacks, and the seventh, twitchings and incontinence. Cohn's [25] first patient had dreamy states and

22. Oppenheim: Zur Kenntnis der Epilepsie und ihrer Randgebiete, Ztschr. f. d. ges. Neurol. u. Psychiat. **42**:352, 1918.

23. Marchand, L.: Des accès épileptiques avec conservation de la conscience, Presse méd. **32**:290, 1924.

24. Friedmann, M.: Zur Auffassung der gehäuften kleinen Anfälle, Monatschr. f. Psychiat. u. Neurol. **38**:76, 1915.

25. Cohn, W.: Ueber gehäufte kleine Anfälle bei Kindern, Monatschr. f. Psychiat. u. Neurol. **46**:106, 1919.

automatic activities; the second, twitchings and amnesia for the attacks; the fourth, twitchings of the facial muscles and unconsciousness during attacks. Meyer's [26] patients were incontinent during the attacks and had amnesia for the seizures. Meyer was able occasionally to demonstrate a Babinski sign during an attack. Stier's [12] first patient showed a sluggish pupillary reaction during the seizures; the second, spasms, and the third, periorbital twitchings; the fourth and fifth patients were unconscious during the attacks; the fifth patient was also incontinent and had fixed pupils; the sixth was incontinent; the twelfth had a clouding of the sensorium; the thirteenth had frank epileptic attacks at the age of 7 years; the fourteenth was incontinent and had amnesia for the attacks, during which the pupils were fixed; the fifteenth had amnesia for the attacks, and the sixteenth had vagovasal attacks from the age of 7 months to that of 6 years following an attack of whooping cough. Pohlisch's [27] first and fifth patients had amnesia for the attacks, and the sixth clonic twitchings. Pohlisch reported 32 cases, in many of which there was evidence of cortical irritation and amnesia. Kochmann's [28] first patient had spasms with unconsciousness and incontinence; the third had clonic twitchings with unconsciousness and incontinence; the fourth was incontinent; the fifth showed grinding of the teeth and clinching of the hands. Adie's [29] patient showed evidence of cortical irritation. Marchand's and Bauer's [30] third patient had amnesia for the attacks; Moreau's [31] second, third, fifth and sixth patients showed some epileptic features; the seventh had convulsions at 15 years and the eighth at 7 and at 9½ years. Ratner's [32] patient whose case was reported in 1930 showed a condition akin to oculogyric crises.

This short review of the clinical manifestations seems to indicate that in many instances the attacks are of the nature of petit mal and that in other cases there is evidence of abortive generalized attacks. In a few cases there was definite indication of an organic reaction, for instance, the evidence of tetany in the second case of Heilbronner,[2] in the case of Mann,[16] in the ninth case of Stier [12] and in the first case of Kochmann.[28] There was a strong possibility of syphilis of the central nervous system in Engelhardt's [8] fourth case and in the third case of Marchand.[30] Finally, there was a definite history of an injury to the head in the sixth case of Sauer [3] and in the second and third cases of Pohlisch.[27] It is important that in certain cases there was evidence

26. Meyer, M.: Zur Klinik und Behandlung der sogenannten gehäuften kleinen Anfälle bei Kindern, Ztschr. f. Kinderh. **27**:293, 1920.

27. Pohlisch, K.: Zur Frage der Pyknolepsie, Arch. f. Psychiat. **67**:424, 1923.

28. Kochmann, R.: Die gehäuften kleinen Anfälle im Kindesalter, Arch. f. Kinderh. **73**:163, 1923.

29. Adie, W. J.: Pyknolepsy: A Form of Epilepsy Occurring in Children with a Good Prognosis, Brain **4**:96, 1924.

30. Marchand, L., and Bauer, L.: Trois cas de pyknolepsie, Bull. Soc. clin. de méd. ment. **14**:29 (March 15) 1926.

31. Moreau, M.: Considération relative à la pyknolepsie, J. de neurol. et de psychiat. **28**:772, 1928.

32. Ratner, J.: Zur Kenntnis der Pyknolepsie und ihrer Grenzgebiete, Arch. f. Psychiat. **89**:802, 1930.

of hydrocephalus, microcephalus and rachitic changes in the bones (Strohmayer [33]).

Considering all these facts it does not seem unreasonable to assume that as regards the pyknolepsies one is dealing with the old problem of general epilepsy. Most of the reasons offered by the various workers for creating a separate entity can hardly stand criticism. The matter, for instance, of the disappearance of the attacks at the time of puberty cannot be considered a sufficient reason for classifying them as a separate entity. There are numerous cases of cryptogenetic epilepsy in which the attacks disappear at puberty, and there are at the same time numerous cases of pyknolepsy in which the attacks persist during adolescence and later. The matter of deterioration has been entirely overemphasized, as if the absence of deterioration in epilepsy were an exception to the rule. Strohmayer [33] has pointed out that only 30 per cent of the patients with epilepsy show evidence of mental deterioration. Furthermore, it is worthy of note that not all the patients with pyknolepsy whose cases have been reported in the literature retained their mental integrity. According to Rosenthal's [34] figures, in 35 per cent of the cases reported up to 1927 the patient showed deterioration to a lesser or greater extent. The lack of therapeutic response to medicinal treatment has been held up by many investigators as a criterion for the consideration of pyknolepsy as an entity which has no relationship to epilepsy. Again, the conclusion was hasty and based on an insufficient number of observations. The patients of Divry,[35] Pohlisch,[27] Marchand [30] and a few other authors have reacted favorably to phenobarbital therapy. Stargardter's [36] patients reacted well to caffeine. Even bromide gave favorable results in some instances, and we feel that sometimes a psychologic approach may be helpful in certain cases.[37] One can say that in pyknolepsy, as in epilepsy in general, some of the patients respond to one and others to another form of therapy, while a number of patients remain refractory to any sort of therapy as, for instance, do epileptic patients with petit mal attacks.

It is futile to go into speculations as to etiology. Less work has been done on this condition than on any of the allied branches of epi-

33. Strohmayer: Die Psychopathologie des Kindesalters, München, J. F. Bergmann, 1923, p. 162.

34. Rosenthal, C.: Zur Frage der gehäuften kleinen Anfälle im Kindesalter, Arch. f. Psychiat. **77**:672, 1926.

35. Divry: A propos du traitement de l'épilepsie par la phénylmalonylurée, Encéphale **17**:169, 1922.

36. Stargardter: Ueber die gehäuften kleinen Anfälle der Kinder, Jahrb. f. Kinderh. **45**:230, 1921.

37. Jelliffe, S. E.: Narcolepsy; Hypnolepsy; Pyknolepsy, M. J. Rec. **129**:269 (March 6); 313 (March 20) 1929.

lepsy. All that can be said at present is that one is probably dealing with the same situation as in cryptogenetic epilepsy and that the attacks are probably closely related to petit mal seizures. In some cases reported in the literature and in our third case there was a definite history of an injury to the head; in other cases there was evidence of a previous inflammatory process in the central nervous system, and in a third group affective instability could be considered as a responsible factor in the lowering of the threshold of convulsibility. There is, however, in addition, some factor which is responsible for the unusual frequency of the pyknoleptic attacks. We are not prepared at the present time to state what this factor is; we can only surmise that some metabolic process may be responsible for the phenomenon. In all probability, as in epilepsy in general, there is a multiplicity of etiologic factors. We, therefore, suggest the existence of various types of pyknolepsy, which, together with the narcolepsies, affect epilepsies and other well known paroxysmal disorders, make up the vast group of convulsive states.

DISTRIBUTION OF BROMIDE IN BLOOD SERUM AND CEREBROSPINAL FLUID

FRANK FREMONT-SMITH, M.D.

MARY ELIZABETH DAILEY, A.B.

AND

DOROTHY H. SLOAN, A.B.

BOSTON

In 1925 Walter [1] developed a method for determining the distribution ratio of bromide in blood serum and cerebrospinal fluid. After the ingestion of sodium bromide for five days, gold chloride solution was added to protein-free filtrates of blood serum and cerebrospinal fluid, and the resultant brown color was compared in a colorimeter to determine the "ratio" of the bromide in the blood serum to that in the cerebrospinal fluid. On the basis of this gold chloride test, or minor modifications of it, a number of articles have been written concerning the permeability to bromide of the meninges or of the blood-cerebrospinal fluid barrier. Many authors report that the test is a valuable diagnostic aid. Some attach considerable theoretical significance to this test in understanding the pathologic physiology of diseases of the nervous system.

Walter made no critical survey of the accuracy of his method. Katzenelbogen and Goldsmith [2] discovered that from 10 to 18 per cent of the sodium bromide added to serum in vitro could not be recovered by the gold chloride method. Mishkis,[3] in a series of four cases, compared the distribution ratios of bromide in blood serum and cerebrospinal fluid determined by the gold chloride method with those determined electrometrically. He found wide discrepancies between the results obtained by the two methods.

We determined the distribution ratios of bromide in blood serum and cerebrospinal fluid both by the gold chloride method of Walter, as modified by Hauptmann, and by the method of Toxopeus [4] in twenty-one instances (eight patients). The data form the basis for this paper.

From the Neurologic Unit, Boston City Hospital, and the Department of Neuropathology, Harvard Medical School.

1. Walter, F. K.: Ztschr. f. d. ges. Neurol. u. Psychiat. **95**:522, 1925.

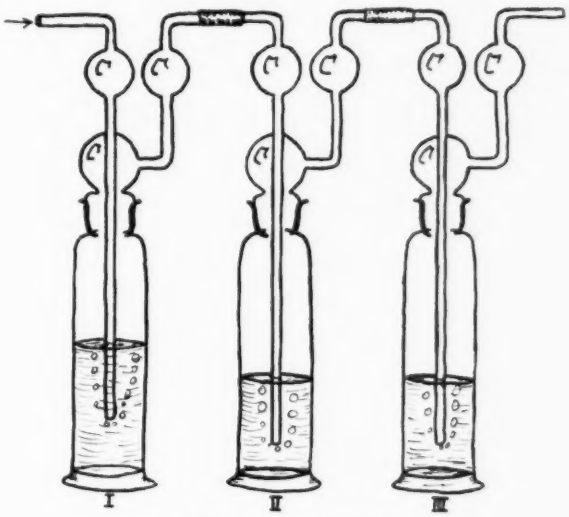
2. Katzenelbogen, S., and Goldsmith, H.: Am. J. Psychiat. **10**:1045, 1931.

3. Mishkis, M.; Ritchie, E. B., and Hastings, A. B.: Proc. Soc. Exper. Biol. & Med. **30**:473, 1933.

4. Toxopeus, M.: Arch. f. exper. Path. u. Pharmakol. **149**:263, 1930.

METHODS

We used the Hauptmann modification of the Walter gold chloride method exactly as described by Malamud.[5] For the quantitative determination of bromide in blood serum and cerebrospinal fluid, we used the method of Toxopeus [4] which is based on the old Berglund method—a selective oxidation of bromide, in the presence of chloride, by potassium permanganate and potassium pyrosulphate. We made a few minor modifications in the method. The exact procedure we used follows: Ten cubic centimeters (or less if 10 cc. is not available) of whole blood, serum or spinal fluid is put in a 300 cc. Erlenmeyer flask, and 10 cc. of two-tenths-normal silver nitrate solution are first added and subsequently 20 cc. of concentrated nitric acid. Small amounts of a saturated solution of potassium permanganate are added several times, and the mixture is boiled until the supernatant fluid is clear and colorless or light yellow. Owing to the low protein content of spinal fluid, very little permanganate is needed in the oxidation process. After digestion the clear solution is allowed to cool slowly in the dark. It is then filtered through ash-free Schiller and Schull filter paper and the precipitate is washed until no acid appears in the wash water. The precipitate, containing the total bromide and chloride as silver chloride and silver bromide, is washed into a beaker and the filter paper broken up and added. Sodium hydrosulphate ($Na_2S_2O_4$) is added from the tip of a knife, about 20 cc. of water is poured in, and the mixture is well stirred for several minutes and let stand for an hour. All the chloride and bromide go into solution as sodium bromide and sodium chloride, and metallic silver is left. The solution of sodium bromide and sodium chloride is filtered off the silver into a 200 cc. volumetric flask, washed several times and made up to volume.



Apparatus employed.

5. Malamud, W.; Fuchs, D. M., and Malamud, N.: Barrier Between the Blood and the Cerebrospinal Fluid, Arch. Neurol. & Psychiat. **20**:780 (Oct.) 1928.

Fifty cubic centimeters of this solution is put in flask I (figure). To this is added 40 cc. of saturated potassium permanganate solution. In flasks II and III are put 75 and 25 cc., respectively, of a solution consisting of 0.08 per cent sodium carbonate and 0.4 per cent sodium thiosulphate. The flasks are closed, and air is run through. To the first flask is added 20 cc. of a 10 per cent solution of potassium pyrosulphate ($K_2S_2O_7$) containing 0.4 per cent sodium carbonate. All the bromide and part of the chloride are oxidized to free bromine and chlorine and go over to the second and third flasks. This stage is allowed to run for two hours. The content of flasks II and III are then combined and evaporated to approximately 20 cc. and washed back into flask I. Then 100 and 30 cc. of a 3 per cent solution of potassium iodide are put in flasks II and III, respectively. The system is closed and 50 cc. of saturated potassium permanganate and 40 cc. of the potassium pyrosulphate solution are added to flask I. Air is run through the system for two hours. The small amount of chlorine present will not go over. The iodine liberated by the bromide in flasks II and III is titrated with two hundredth-normal sodium thiosulphate, starch being used as an indicator. The thiosulphate solution is standardized against sodium biiodate.

TABLE 1.—*Recovery of Added Bromide*

	Bromide Added, Mg. per 100 Cc.	Bromide Recovered, Mg. per 100 Cc.
0.7 per cent sodium chloride	195	190
	195	195
Spinal fluid	91	88
	130	128
Blood serum	130	130
	200	200
	200	201
Whole blood	286	281

Realizing the theoretical objections to the absolute reliability of any method for the determination of bromide in the presence of chloride, two of us, working independently, checked each other's results in the recovery of added bromide before proceeding to study the actual distribution between blood serum and cerebrospinal fluid.

Varying known amounts of sodium bromide were added to a 0.7 per cent solution of sodium chloride, to spinal fluid, to blood serum and to whole blood. The recovery of the added bromide (table 1) assured us that the method was reliable in our hands and sufficiently exact for our purposes.

In our series, seven patients were given 0.01 Gm. of sodium bromide per pound of body weight three times a day. The number of days of ingestion of bromide varied in different experiments. Blood was collected under oil from seventeen to nineteen hours after the last dose and after a fast of from sixteen to eighteen hours. The lumbar puncture was performed under procaine anesthesia immediately after the blood sample had been taken. We collected as large an amount of spinal fluid as was reasonable in each instance, approximately 30 cc. of spinal fluid, and mixed it well before taking samples for determinations.

RESULTS

The results of nineteen comparative determinations of bromide in blood and cerebrospinal fluid of seven patients who had ingested bromide

for several days and the results of two such determinations for a patient with bromide poisoning are presented in table 2. In nearly all instances the determinations were made in duplicate, both figures being given.

TABLE 2.—*Distribution of Bromide Between Blood Serum and Cerebrospinal Fluid as Determined by the Method of Toxopeus*

Case	Diagnosis	Number Days Receiving Sodium Bromide	Serum, Mg. Bromide per 100 Cc.	Spinal Fluid, Mg. Bromide per 100 Cc.
1	Multiple sclerosis	3	33	12
			32	11
		5	55	13
			56	15
		7	78	37
			79	36
2	Dementia paralytica	3	41	17
				17
		5	62	27
			67	26
		7	72	37
				39
3	Epilepsy	3	32	5
			34	8
		5	53	14
			52	
		7	68	26
4	Dementia paralytica	4	46	22
			44	22
		5	52	25
			54	24
		6	49	18
5	Multiple sclerosis	5	46	20 Sample 1
			47	19 (12 cc.)
				18 Sample 2
				18 (11 cc.)
			(7 cc. removed between these samples)	
		Days After Discontinuing Sodium Bromide		
6	Arteriosclerotic heart disease	1	54	23
			52	21
	(Bromide administered for 5 days)	3	44	20
			46	18
		5	42	17
			44	19
7	General arteriosclerosis with cerebral softening	1	47	18
			49	18
	(Bromide administered for 5 days)	3	45	18
			42	18
		5	38	13
			37	11
8	Bromide poisoning	1	290	193
		11	87	38
			85	35

It will be seen that with four exceptions the duplicate determinations checked within 2 mg., the greatest discrepancy being 5 mg. in the blood serum in case 2 on the fifth day. In cases 1, 2 and 3, the bromide was administered for seven days. Samples of blood and cerebrospinal fluid were taken when the patient was fasting, from fifteen to seventeen hours after the end of the third, fifth and seventh days of administra-

tion of bromide. In every instance there was a steady rise in the bromide content of both the serum and the cerebrospinal fluid throughout the experiment. The cerebrospinal fluid value was always lower than that of the blood serum and sometimes considerably lower. In case 4 the samples were taken on the fourth, fifth and sixth days. In this case there was a rise in bromide in blood and cerebrospinal fluid between the fourth and the fifth day, and a fall in both between the fifth and the sixth day.

In cases 6 and 7, the administration of bromide was discontinued at the end of five days and samples of serum and cerebrospinal fluid were taken on the first, third and fifth days thereafter. In both cases, there was a steady fall in the bromide content of the blood serum and of the cerebrospinal fluid, although in case 7 the amount in the cerebrospinal fluid remained unchanged on the third day after the administration of bromide was discontinued. Here again, the bromide content of the cerebrospinal fluid was at all times considerably less than that of the blood serum. In case 5 samples of blood and cerebrospinal fluid were withdrawn after five days of administration of bromide, and the cerebrospinal fluid was divided as follows: The first 12 cc. removed was used for sample 1, the next 7 cc. was discarded, and a final 11 cc. was used for sample 2. The second sample contained about 1 mg. less bromide per hundred cubic centimeters than the first sample. This is too small a difference to be of significance, but it is in accordance with the results of Fleischacker and Scheiderer,[6] who found decreasing amounts of bromide in successively removed samples of cerebrospinal fluid, and with those of Schönfeld and Leipold,[7] who found more bromide in the lumbar fluid than in the cistern fluid at combined lumbar and cistern puncture. These investigators used the gold chloride method.

Case 8 was that of a patient who had been taking from twenty-four to forty-eight 10 grain tablets of the bromides of sodium, potassium and ammonium each day for five weeks. The first sample of blood and cerebrospinal fluid were obtained on the day after admission and the second samples ten days later (i. e., eleven days after discontinuing bromide). This case showed the highest bromide values in our series. The bromide content of the blood serum was considerably higher than that of the cerebrospinal fluid, but the ratio was smaller than in the other cases.

In table 3, the ratios of serum to cerebrospinal fluid bromide obtained by the method of Toxopeus are compared with the ratios obtained by

6. Fleischacker, H., and Scheiderer, G.: (*a*) Ztschr. f. d. ges. Neurol. u. Psychiat. **116**:692, 1928; (*b*) Monatschr. f. Psychiat. u. Neurol. **75**:346, 1930; (*c*) Deutsche med. Wchnschr. **56**:1657, 1930.

7. Schönfeld, W., and Leipold, W.: Ztschr. f. d. ges. Neurol. u. Psychiat. **95**:473, 1925.

the gold chloride method on the same samples of blood and cerebrospinal fluid. The ratios obtained by the Toxopeus method ranged from 1.5 to 4; those obtained by the gold chloride method ranged from 2.3 to 3.6. There was considerable variation in ratios on different days in nearly every experiment. This was true of the ratios obtained by both methods. For instance, in case 1, the ratio obtained by the Toxopeus method on the third day after administration of bromide was 2.8, on the fifth day 4 and on the seventh day, 2.1. In case 6, however, the ratios obtained

TABLE 3.—*Comparison of the Ratio of Serum to Cerebrospinal Fluid Bromide as Determined by the Method of Toxopeus and by the Gold Chloride Method*

Case	Diagnosis	Number Days Receiving Sodium Bromide	Toxopeus	Gold Chloride
1	Multiple sclerosis	3	2.8	3.0
		5	4.0	2.4
		7	2.1	2.6
2	Dementia paralytica	3	2.4	2.8
		5	2.4	2.9
		7	1.9	2.6
3	Epilepsy	3	4.7	3.6
		5	3.8	3.5
		7	2.6	2.4
4	Dementia paralytica	4	2.1	2.6
		5	2.1	2.4
		6	2.7	2.3
5	Multiple sclerosis	5	(Sample 1) 2.4	2.8
			(Sample 2) 2.6	2.6
		(7 cc. removed between these samples)		
		Days After Discontinuing Sodium Bromide		
6	Arteriosclerotic heart disease	1	2.4	2.6
		3	2.4	2.3
		5	2.4	2.9
7	General arteriosclerosis with cerebral softening	1	2.7	2.5
		3	2.4	2.8
		5	3.2	2.9
8	Bromide poisoning	1	1.5	2.8
		11	2.3	3.0

by the Toxopeus method were constant throughout the test. It was also evident that there was a marked difference between the ratios obtained by the gold chloride method and those obtained by the Toxopeus method. Furthermore, there was no consistency in this discrepancy because while the ratio determined by the Toxopeus method was moving in one direction the ratio determined by the gold chloride method might be moving in the opposite direction. For instance, in case 1, the ratio obtained by the Toxopeus method between the third and the fifth day changed from 2.8 to 4, while the corresponding ratio obtained by the gold chloride method varied in the opposite direction, from 3 to 2.4. In the same case, between the fifth and the seventh day, the ratio determined by the Toxopeus method fell from 4 to 2.1, while in the same

time the ratio obtained by the gold chloride method rose from 2.4 to 2.6. In case 6, in which the ratio determined by the Toxopeus method remained constant at 2.4, the ratio determined by the gold chloride method moved from 2.6 to 2.3 and then to 2.9. In only one instance, case 7 (sample 2), were the ratios obtained by the two methods identical. In case 1 there was a ratio of 4 (Toxopeus method) as compared to a ratio of 2.4 (gold chloride method), while two days later the ratios were 2.1 and 2.6 for the Toxopeus and the gold chloride method, respectively.

COMMENT

It is evident from the data presented in table 3 that there is a marked discrepancy in the distribution ratios obtained by these two methods. This discrepancy is similar to that observed by Mishkis.[3] The Toxopeus method is a standard quantitative method for the determination of bromide in the presence of chloride. Two of us working independently were able to recover bromide accurately from salt solution, blood serum, whole blood and cerebrospinal fluid, as indicated in table 1. This, together with the fact that our duplicate analyses in the experiments shown in table 2 nearly always checked within 2 mg., gives us assurance of the reliability of the method in our hands.

The gold chloride method depends on the comparison of the brown color obtained on adding gold chloride solution to protein-free filtrates of blood and cerebrospinal fluid. The results are expressed not in milligrams but as distribution ratios. This method is open to a number of objections. First, the exact composition of acid gold chloride is unknown.[8] It is probable that it is composed of a mixture of several gold salts. There is no assurance that the proportion of these salts is the same in different samples. It is unlikely that each of these salts gives the same degree of color when added to a solution containing bromide. Second, Katzenelbogen and Goldsmith [2] found that from 10 to 18 per cent of sodium bromide added to serum in vitro could not be recovered by the gold chloride method. Third, the influence of the chloride ions present on the color developed when gold chloride is added to a solution of bromide has been neglected. When a solution of gold chloride is added to a simple bromide solution there are many possible reactions, and the color produced is limited to the extent to which the various possible reactions go to completion. According to the law of mass action the presence of chloride ions causes a tendency to the reversal of these reactions. Actually, when equal amounts of the same gold chloride solution are added to solutions identical in bromide con-

8. Mellor, J. W.: Inorganic and Theoretical Chemistry, New York, Longmans Green & Company, 1923, vol. 3, p. 588.

centration but differing in chloride content the color produced varies inversely as the chloride concentration. The influence of chloride ions is particularly important (*a*) because the cerebrospinal fluid normally has a considerably higher concentration of chloride than has the blood serum and (*b*) because the usual technic for the gold chloride method calls for a greater dilution of the serum than of the cerebrospinal fluid in order to make the colors obtained comparable. The serum (but not the cerebrospinal fluid) is diluted with 2 volumes of water before trichloracetic acid is added to precipitate the protein, the final dilutions of the serum being 1 : 3.6 while the final dilution of spinal fluid is only 1 : 1.2. This means that the level of chloride ions in the serum, originally lower than that in the cerebrospinal fluid, is further decreased by this procedure. Since the intensity of color produced varies inversely as

TABLE 4.—*Effect of Chloride Concentration on the Apparent Ratio of Serum to Cerebrospinal Fluid Bromide as Determined by the Gold Chloride Method*

Hauptmann Modification of Walter Gold Chloride Method	Spinal Fluid Diluted With Water
1.5	1.4
1.6	1.4
1.7	1.6
2.8	2.0
2.8	1.7
2.9	2.0
3.1	2.3
	Serum Diluted with 0.8% Sodium Chloride
2.8	2.6
2.8	2.2
3.0	2.4
2.9	2.5

the chloride concentration, it is evident that the excess chloride ions in the spinal fluid filtrate tend to inhibit the formation of color. This results in an apparently lower bromide content in the cerebrospinal fluid than is actually present.

In order to demonstrate the effect of the chloride ion, we compared the ratio determined in the usual way with the ratio obtained when the spinal fluid as well as the serum was diluted with 2 volumes of water. Seven such comparative studies are shown in table 4. In every instance the dilution of the spinal fluid as well as the serum with water resulted in a lower ratio of serum to spinal fluid bromide than when only the serum was so diluted; i. e., the dilution of the spinal fluid with water made the chloride concentrations of the two filtrates more nearly alike and prevented the inhibiting effect on the color of the excess chloride in the serum filtrate. We also demonstrated the influence of the chloride ion in another way, i. e., by diluting the serum with 2 volumes of 0.8 per cent sodium chloride solution instead of with water, the spinal fluid

being undiluted. The ratios so obtained were compared with the ratios obtained when the serum was diluted with 2 volumes of water in the usual way. Four such comparisons are presented in table 4. Here again the equalization of the level of chloride ions in the two filtrates led to significantly lower ratios in every instance. These two observations prove that the gold chloride method, as usually used, has a very appreciable error owing to the difference in the concentrations of chloride ions in the filtrates of blood and cerebrospinal fluid. This difficulty is not easy to compensate for completely unless one knows accurately the original chloride concentration of both the blood serum and the cerebrospinal fluid and dilutes them so that the chloride concentration in the two filtrates to which gold chloride is to be added is identical. As there are appreciable individual variations in the distribution of chloride between blood and cerebrospinal fluid, as the administration of sodium bromide causes a disturbance in the chloride equilibrium within the body and a displacement of chloride from the body and as this effect is appreciably influenced by the chloride and water content of the diet and perhaps by other unknown factors, it appears that there is a significant uncontrolled error in the gold chloride method. We feel, therefore, that the discrepancies noted between the ratios obtained by the Toxopeus method and those obtained by the gold chloride method must be ascribed largely to the unreliability of the gold chloride method.

It is not our purpose in this paper to discuss in any detail the clinical application of the gold chloride method either to diagnosis or to interpretation of the pathogenesis of disease. We reviewed fourteen papers [9] which contained the results of more than three thousand determinations of the distribution ratio by the gold chloride method. Only four of the authors presented any values for normal subjects, the two largest groups of "normals" being a series of forty-eight reported by Walter [9a]

9. (*a*) Walter, F. K.: Die Blut-Liquorschranke; Leipzig, Georg Thieme, 1929. (*b*) von Rohden, F.: Arch. f. Psychiat. **87**:797, 1929. (*c*) Hauptmann, A.: Ztschr. f. d. ges. Neurol. u. Psychiat. **100**:332, 1925; Monatschr. f. Psychiat. u. Neurol. **68**:243, 1928. (*d*) Sunderhauf, R.: Ztschr. f. d. ges. exper. Med. **55**:378, 1927. (*e*) Malamud, W., and Wilson, R. B.: Paresis Treated with Malaria, Arch. Neurol. & Psychiat. **22**:1135 (Dec.) 1929. (*f*) Malamud, W., and Rothschild, D.: Barrier Between the Blood and Cerebrospinal Fluid: III. Distribution and Ratio of Bromides in Schizophrenia, Arch. Neurol. & Psychiat. **24**:348 (Aug.) 1930; The Blood-Cerebrospinal Fluid Barrier in Manic-Depressive Psychosis; Ratios of Distributing Bromide Calcium, Sugar and Chloride, ibid. **26**:829 (Oct.) 1931. (*g*) Katzenelbogen, S.: J. Nerv. & Ment. Dis. **75**:144, 1932. (*h*) Gordy, S. T., and Smith, S. M.: Permeability of the Hemato-Encephalic Barrier as Determined by the Bromide Method, Arch. Neurol. & Psychiat. **24**:727 (Oct.) 1930. (*i*) Bauman, C.: Monatschr. f. Psychiat. u. Neurol. **81**:241, 1932. Katzenelbogen and Goldsmith.[2] Malamud, Fuchs and Malamud.[5] Fleischacker and Scheiderer.[6b]

and thirty-five in a total of twelve hundred and fifty determinations by von Rohden.[9b] Walter arbitrarily chose the limits of the normal ratio as ranging from 2.9 to 3.5 (in an earlier paper he used 2.9 to 3.3), in spite of the fact that three of his forty-eight values for normal subjects were outside of these limits. Von Rohden arbitrarily chose from 2.9 to 3.3 for the normal limits although his values for normal subjects ranged from 2.6 to 3.3. It would seem necessary to establish the normal range for the bromide ratio in a large series of normal subjects by a reliable method before the results for patients with the various psychoses and other diseases of the central nervous system can be evaluated. We feel that the data on normal values in the literature are inadequate.

Moreover, in order to accept bromide ratios as an index of permeability of the meninges for bromide, it is necessary to know that the bromide has reached an equilibrium in its distribution between the blood serum and the cerebrospinal fluid at the time the two samples are taken. From our data it is evident that on the fifth day after administration of bromide the bromide contents of the blood serum and cerebrospinal fluid were still rising (cases 1, 2 and 3). In case 4, however, the bromide content of both the blood serum and the cerebrospinal fluid fell slightly between the fifth and the sixth day in spite of continued administration. These observations indicate that the bromide had not reached equilibrium on the fifth day, as do the observations already mentioned that the later samples of cerebrospinal fluid, or fluid from the cisterna magna, contained more bromide than the first fluid removed from the lumbar sac.

It is necessary, therefore, to have not only a reliable method for determining bromide but a method for administering it which will assure equilibrium at the time the permeability of the meninges is to be studied. The control of the chloride and the water content of the diet is probably important in this regard.

The theoretical significance of the higher content of bromide in the blood serum than in the cerebrospinal fluid, in contradistinction to the reverse relationship for chlorides, needs further study and will be discussed in another communication.

SUMMARY

1. The bromide content of the blood serum and the cerebrospinal fluid after administration of bromide was determined quantitatively in a small series of patients by the method of Toxopeus.

2. The distribution ratios of bromide in blood serum and cerebrospinal fluid as obtained by the gold chloride method had no correlation with the ratios obtained in the same cases by the quantitative method of Toxopeus.

3. When sodium bromide is administered according to Hauptmann's modification of Walter's method for a period of from three to seven days, the bromide content of the blood serum is at all times appreciably higher than that of the cerebrospinal fluid, the ratios varying from 1.9 to 4.7 in our cases.

4. The gold chloride method is not sufficiently accurate for the determination of the distribution ratio of bromide in blood serum and cerebrospinal fluid.

5. The normal range for the distribution ratio of bromide in blood serum and cerebrospinal fluid has not been established.

BODY TEMPERATURES OF PERSONS WITH SCHIZOPHRENIA AND OF NORMAL SUBJECTS

EFFECT OF CHANGES IN ENVIRONMENTAL TEMPERATURE

JACQUES S. GOTTLIEB, M.D.
AND
FORREST E. LINDER, PH.D.
WORCESTER, MASS.

Since it has been shown that schizophrenia is characterized by a variability greater than normal in certain physiologic processes and thus possibly that patients with this condition do not comply adequately with homeostatic principles,[1] the general question of the effective adaptiveness of these patients to the external environment becomes pertinent. Normal man, as a homothermic animal, is able to preserve the constancy of his body temperature within a limited range regardless of a moderate amount of change in the external environment. The inability to maintain a constant body temperature, or poikilothermism, is definitely abnormal and indicative of a loss of some of the higher protective mechanisms of the body. The purpose of this investigation was to ascertain whether or not patients with schizophrenia could adapt themselves to changes in the external environment as regards body temperature, pulse and blood pressure as readily as could normal controls. This report deals only with the effect of sudden changes in the environmental temperature and the associated relative humidity on the oral and rectal temperatures of schizophrenic patients and normal subjects.

METHOD

The investigation was conducted in a brick-lined, windowless, cylindric room, 13 feet (396.2 cm.) in diameter by 8 feet (243.8 cm.) in height. The room was heated by eight electric heaters, four on the floor and four on the ceiling, all pointing toward the walls and arranged equidistant from each other. Ventilation was maintained by means of an electric suction fan near the floor and was controlled by a rheostat. Opposite the fan near the ceiling was the fresh air inlet, about 1 foot (30 cm.) square, having a wooden flange in front to prevent direct air currents from circulating in the chamber. Two beds were arranged symmetrically with respect to the heaters and ventilating fan.

The room temperature was measured by a thermometer the accuracy of which was within its reading error of 0.3 F. It was kept at a point approximately

From the research service of the Worcester State Hospital and the Memorial Foundation for Neuro-Endocrine Research.

1. Hoskins, R. G., and Sleeper, F. H.: Organic Functions in Schizophrenia, Arch. Neurol. & Psychiat. **30**:123 (July) 1933.

midway between the two beds and on a level with them. A sling psychrometer was suspended in front of the ventilation fan so that measurements of relative humidity could be obtained.

Two subjects, either normal or schizophrenic, were observed at a time. They were brought to this experimental chamber in a nonfasting state soon after the midday meal. All experimental periods began between 1:15 and 1:45 p. m. and lasted for three and one-half hours. The subjects undressed completely and lay quietly on the beds during the entire period. The room temperature at the beginning of each experimental day was 74.3 ± 0.75 F. After the first half-hour and every half-hour thereafter, observations of the room temperature and the relative humidity of the room, the rectal temperature, the oral temperature, the systolic and the diastolic blood pressure, the pulse pressure and the pulse rate were recorded. This gave a series of seven successive observations during the three and one-half hour period for each of the eight variables measured.

The body temperature was taken with paired clinical rectal thermometers, accurate within their reading error of 0.1 F., which had been matched by comparison with a standard laboratory thermometer in a water bath, as described by Carmichael and Linder.[2] Precautions were taken as follows: The same thermometers were used throughout for each subject; they were inserted in the body cavities to a depth of approximately 5 cm. and were left for ten minutes; care was taken that the lips were kept firmly together and that there was no rubbing with the tongue.

Each subject came to the experimental room on two occasions. One time, usually the first, the room temperature was maintained at 74.3 ± 0.75 F. On the second day, immediately after the first set of observations, the room temperature was raised rapidly from the general level of 74.3 F. so that at the end of the three and one-half hour period it was approximately 92.5 F. Thus, there were two experimental days: one, called hereafter the "constant heat day," in which the environment was kept the same throughout the period of the experiment, and the other, referred to as the "varied heat day," in which the environment was rapidly changed.

Forty-two subjects were submitted to this procedure. Twenty-six of them were patients with schizophrenia and sixteen were normal controls. The schizophrenic patients were men varying in age from 17 to 48 years, who showed no discernible foci of infection or disease of the upper respiratory tract. The sixteen normal controls were men ranging in age from 20 to 32, members of the staff, laboratory technicians and medical students, who were in good health and without infection of the upper respiratory tract.

Precautions were taken with regard to certain factors which might have invalidated the results. The effect of preexperimental conditions probably would be similar on the average if large enough groups of patients and normal subjects were interspersed among each other at random. On the morning of the test days both groups had approximately the same amount of exercise within the hospital, ate similar food and were exposed to a similar environment. The postabsorptive period for both groups was approximately an hour before the tests began. Since the collection of data took from August through January, any gross effect of season or time was minimized by the haphazard interspersion. Certain environmental

2. Carmichael, H. T., and Linder, F. E.: The Relation Between Oral and Rectal Temperatures in Normal and Schizophrenic Subjects, Am. J. M. Sc. **188**: 68, 1934.

factors, such as radiation from heaters and walls and the effect of air currents, would be small in their variation and similar in their means for the two groups of subjects.

During the early part of the experiment either two patients or two normal persons were studied together, but after observations had been made on twenty patients and ten normal controls each additional patient was studied at the same time as was a normal subject. Thus, two groups of data have been obtained, the statistical consistency of which contributes to the reliability of the general results.

In table 1 are the means of the room temperature for the successive half-hour periods as maintained on both the constant and the varied heat day for both the patients and the normal subjects. On the constant heat day the mean room temperature was held between 74.34 and 74.88 F. On the varied heat day the mean room temperature increased at about the same rate for both patients and normal controls.

The means for the relative humidity of the room as given in table 1 show that on the constant heat day there was a 2 per cent difference between the two groups

TABLE 1.—*Mean Room Temperature and Relative Humidity for Normal Controls and Patients on Each Experimental Day*

	Successive Half Hour Periods						
	1	2	3	4	5	6	7
Constant heat day, room temperature, F.							
Controls	74.88	74.87	74.66	74.68	74.70	74.74	74.50
Patients	74.50	74.36	74.52	74.34	74.68	74.59	74.52
Varied heat day, room temperature, F.							
Controls	74.48	81.82	86.00	88.79	90.59	91.67	91.67
Patients	74.72	81.35	86.63	89.12	91.04	92.15	92.66
Constant heat day, relative humidity							
Controls	44.5	43.3	43.1	43.0	42.7	42.3	43.2
Patients	46.5	46.0	45.2	45.4	45.3	45.0	45.0
Varied heat day, relative humidity							
Controls	43.1	33.3	32.9	31.5	31.9	31.1	30.9
Patients	45.6	34.2	34.5	34.5	34.2	34.8	35.2

of data during the entire observation period. On the varied heat day the difference, beginning with 2.5 per cent, increased to 4.3 per cent at the end of the period of observation. The means for the patients on both days were higher. On the varied heat day there was a marked drop, of about 10 per cent, in the relative humidity from the first to the second period, which was a result of the increase in the room temperature at that time. These small differences have led to an analysis of the effect of relative humidity on the measured physiologic variables, from which it was evident that the comparisons of the data for patients and those for normal subjects were not thereby invalidated.

The data collected on the two experimental days have been subjected to a rigid statistical analysis. Here are presented only a few of the more pertinent facts, indicating differences between the reaction of normal and that of schizophrenic subjects to a controlled environment. The significance of any such difference observed has been tested by Fisher's method of analysis. The probability (P) thereby obtained indicates the relative frequency with which a result similar to the one obtained would occur by chance.[3] Since the usual criterion for significance

3. Fisher, R. A.: Statistical Methods for Research Workers, London, Oliver & Boyd, 1930, p. 104.

requires a P not greater than 0.02, all of the significant findings, unless stated specifically, are based on a P of this value or less. The word "significance" will hereafter be used only with statistical connotation.

OBSERVATIONS

Chart 1 shows the time sequence of the mean rectal and oral temperatures for both the patients and the normal subjects for the three and one-half hour period on the constant heat day. The mean values plotted on these graphs are given in table 2. Statistical comparisons between the patients and the controls show that at no point of either the rectal or the oral curves are there significant differences between the groups. In spite of this similarity in the general level, the curves are somewhat different in certain respects.

The mean rectal temperature for the normal subjects, beginning above that of the patients, showed a significant drop of 0.38 F. during

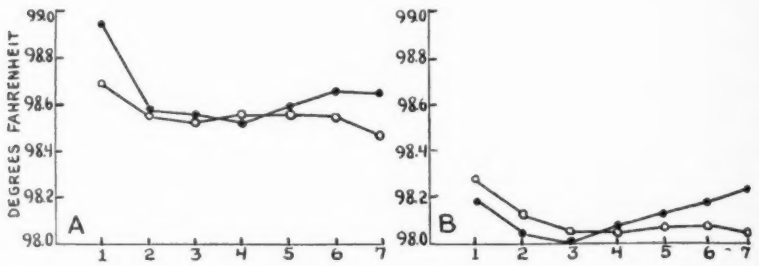


Chart 1.—The time sequence in successive half hour periods of the mean rectal (A) and oral (B) temperature for both patients and normal subjects on the constant heat day. The mean room temperature was maintained between 74.34 F. and 74.88 F. for the entire three and one-half hour period of observation. In this and the following figures the line with the solid circles indicates the record for the normal controls, and the line with open circles, that for the patients.

the first half-hour and then remained at about the same general level until from the fifth to the seventh half-hour period, when there was a slight significant rise. The change for the entire period of observation was a significant fall of 0.32 F. This difference was entirely dependent on the initial drop. The mean rectal temperature for the patients dropped 0.13 F. during the first half-hour. This drop was significant, but was only one-third as great as that for the normal subjects. In contrast to the terminal rise for the normal subjects, the curve for the patients shows an insignificant terminal drop of 0.08 F. The change for the entire period of observation was a significant drop of 0.22 F. This drop, however, was dependent on the summation of the initial and terminal falls.

The mean oral temperature for the normal controls began lower than that for the patients. The initial drop of 0.17 F. during the first hour approaches significance ($P < 0.05$). For the remainder of the three and one-half hour period there was a gradual rise, so that at the terminal reading the mean oral temperature was slightly above the initial value. The mean oral temperature of the patients underwent a significant drop of 0.23 F. during the first hour. After this initial

TABLE 2.—*Mean Body Temperature of Normal Controls and of Patients on Each Experimental Day*

	No. in Group	Successive Half Hour Periods						
		1	2	3	4	5	6	7
Constant heat day								
Rectal temperature, F.								
Patients	26	98.69	98.56	98.53	98.55	98.57	98.55	98.47
Controls	16	98.96	98.58	98.56	98.54	98.58	98.66	98.64
Oral temperature, F.								
Patients	26	98.27	98.13	98.04	98.05	98.07	98.08	98.05
Controls	16	98.18	98.03	98.01	98.06	98.13	98.18	98.23
Varied heat day								
Rectal temperature, F.								
Patients	26	98.69	98.47	98.56	98.77	98.94	99.05	99.11
Controls	16	98.89	98.54	98.52	98.60	98.74	98.85	98.93
Oral temperature, F.								
Patients	26	98.25	98.05	98.26	98.48	98.60	98.67	98.72
Controls	16	98.24	98.04	98.12	98.25	98.38	98.52	98.59
Increment between varied and constant heat day								
Rectal temperature, F.								
Paranoid persons	5	0.10	0.02	0.20	0.48	0.76	0.82	0.92
Nonparanoid persons	21	−0.02	−0.11	−0.01	0.17	0.29	0.43	0.58
Patients	26	0.00	−0.09	0.04	0.23	0.38	0.51	0.65
Controls	16	−0.06	−0.03	−0.04	0.06	0.16	0.19	0.29
Oral temperature, F.								
Paranoid persons	5	0.12	0.14	0.54	0.76	0.96	1.04	1.08
Nonparanoid persons	21	−0.06	−0.14	0.15	0.36	0.43	0.47	0.58
Patients	26	−0.02	−0.09	0.22	0.44	0.54	0.58	0.67
Controls	16	0.06	0.01	0.11	0.19	0.25	0.34	0.36
Rectal-oral differential								
Constant heat day, F.								
Patients	26	0.42	0.43	0.49	0.50	0.50	0.46	0.41
Controls	16	0.78	0.54	0.55	0.48	0.44	0.48	0.41
Varied heat day, F.								
Patients	26	0.44	0.43	0.30	0.29	0.34	0.39	0.39
Controls	16	0.65	0.51	0.40	0.35	0.36	0.33	0.34

drop there was no compensating increase such as was found in the case of the normal controls.

The means of the rectal and oral temperatures for both the patients and the normal subjects throughout the three and one-half hour period on the varied heat day are given in table 2 and plotted in chart 2. On the constant heat day the initial drops in rectal and in oral temperature were significant for both the patients and the normal subjects. On the varied heat day these falls occurred during the sharpest rise in environmental temperature. Yet in spite of the environmental changes, the drops were similar in magnitude on both days.

On examining the curves of the mean rectal temperature one notes that there was a subsequent rise after the initial fall for both the patients and the normal subjects. The gradual but significant rise of 0.39 F. for the normal controls terminated at a level which was only a trifle higher than the initial reading. Thus there was no significant change from the first to the seventh period. The mean rectal temperature of the patients rose much more rapidly after the initial fall. The increase of 0.64 F. is significant and sufficient to bring the terminal reading to a significant level above the initial value.

The curves of the mean oral temperature reveal similar results. The subsequent rise after the initial fall was greater for the patients than for the normal subjects. The normal controls had a rise of 0.55 F. from the second to the seventh period, so that for the entire period of observation there was a significant increase of 0.35 F. After the initial

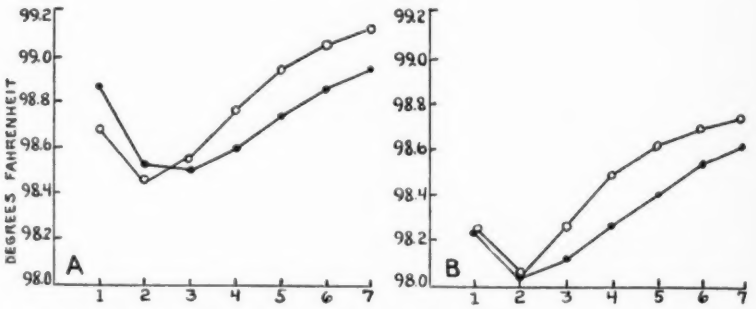


Chart 2.—The time sequence of the mean rectal (*A*) and oral (*B*) temperature for both patients and normal subjects on the varied heat day. The approximate mean room temperatures for the seven successive half-hour periods were: 74.5, 81.5, 86.25, 89, 90.75, 91.75 and 92 F.

fall the mean oral temperature of the patients rose 0.67 F. The difference of 0.47 F. between the first and the last value is significant.

The total effect of increased environmental temperature can be seen only by contrasting the body temperature on the constant heat day with the corresponding temperature on the varied heat day. The values shown in chart 3 were obtained by subtracting each mean for the constant heat day from the corresponding mean for the varied heat day. The curves thereby obtained indicate the effect which can be attributed only to the difference in the controlled environmental situation on the two experimental days. These values, showing the resultant effect of increased environmental temperature, will be referred to as "heat increments" or simply as "increments." The mean increments plotted in chart 3 are given in table 2.

The initial rectal increment for the normal subjects was —0.06 F., and the final value was 0.29 F. For the patients the initial increment was 0 F., and the final value was 0.65 F. The changes in both cases are significant. Likewise, the difference of 0.36 F. between the increment of the patients and that of normal controls at the seventh reading is significant. The results for the oral temperature heat increment are similar. The normal subjects began with an increment of 0.06 F. which at the final value was 0.36 F. The initial increment for the patients was —0.02 F., which rose to a terminal value of 0.67 F. These changes are significant. A comparison of the value for normal controls and that for the patients at the seventh period yields a difference of 0.31 F., giving a *P* below 0.05 but greater than 0.02. This result, which independently could hardly be called significant, becomes convincing when considered in relation to the other findings. The mean rise of the oral

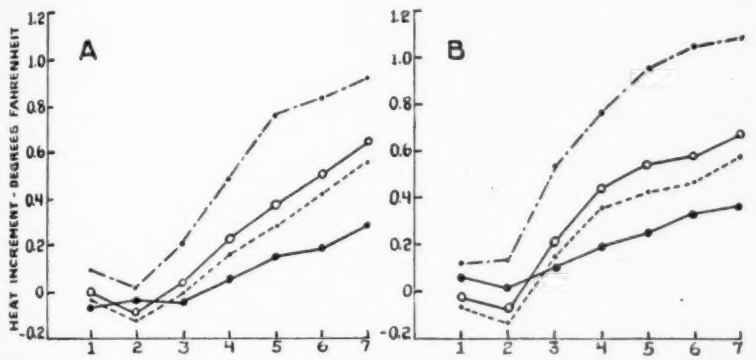


Chart 3.—The time sequence of the differences obtained by subtracting each mean for the constant heat day from the corresponding mean for the varied heat day. These values, referred to as increments (*A*, rectal temperature increment; *B*, oral temperature increment), show the resultant effect of the increased environmental temperature. On the graph are contrasted the mean curves obtained for the normal subjects, all the patients, the paranoid schizophrenic patients (5) and the patients not in the paranoid schizophrenic group. The dash and dot line indicates the record for the paranoid patients, and the dotted line, that of patients not in the paranoid group.

temperature for the patients was almost twice that of the normal subjects.

The heat increments have been obtained for the schizophrenic subgroups. In chart 3 and in table 2 are given the mean values for the paranoid group, which seem to be sharply differentiated from those of the other subgroups. The changes were practically three times as great as were those obtained for the normal subjects. Tests for significance are hardly feasible because of the small number of this subgroup (five).

A definite response of the subgroup seems indicated, which offers a possibility for future investigation.

These curves emphasize the striking difference between the response temperature of the patients and that of the normal subjects to an increase of only 18 F. in the environmental temperature.

COMMENT

While the results of this investigation show differences in the heat-regulating mechanism of the two groups of subjects, definite isolation of the cause of these differences must await further studies. Several possibilities present themselves. Freeman and Hoskins [4] have shown that the blood pressure of schizophrenic patients increases when they are given an extract of suprarenal cortex in glycerin by mouth, whereas control subjects fail to show any increase. This strong suggestion of an insufficiency of the suprarenal cortex is of interest when considered with the work of Hartman, Lockwood and Lockie,[5] who have shown

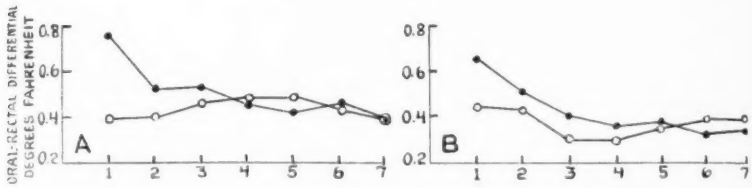


Chart 4.—The time sequence of the mean difference, called differential, between the simultaneous oral and rectal temperatures for patients and normal subjects on each experimental day. *A* gives the record for the constant heat day and *B*, that for the varied heat day.

that suprarenalectomized rats are more affected by an increase in the environmental temperature than are normal rats. Abnormal functioning of the sympathetic nervous system and poor mobilization of tissue water associated with an insufficiency of the suprarenal cortex can affect the heat-dissipating mechanism. The heat center, particularly through the autonomic nervous system, regulates the distribution of the blood as an aid in the maintenance of homothermism. Since it has been shown that removal of the sympathetic nervous system causes a greater reactivity in body temperature,[6] examination of our data for their meaning with reference to blood shifts will be worth while.

4. Freeman, H., and Hoskins, R. G.: Comparative Sensitiveness of Schizophrenic and Normal Subjects to Glycerin Extract of Adrenal Cortex, Endocrinology **18**:576 (Oct.) 1934.

5. Hartman, F. A.; Lockwood, J. E., and Lockie, L. M.: Resistance to Heat in Adrenal Insufficiency, Proc. Soc. Exper. Biol. & Med. **29**:409, 1932.

6. Cannon, W. B.: The Autonomic Nervous System: An Interpretation (Linacre Lecture), Lancet **1**:1109 (May 24) 1930.

The temperature of any particular part of the body is dependent on the heat energy being brought to it or produced in it and on the loss or dissipation of that energy. Although other factors are concerned in the conduction of heat, the necessary gradients are partially dependent on the intervention of the blood supply. Therefore, any changes in temperature are important for the indirect information given as to the nature of the distribution of blood.

Since the initial drops in the means of both oral and rectal temperatures are similar on the constant and varied heat days, they do not seem to be due to the influence of the controlled environmental temperature. They may result from the exposure of the nude body to the environment, from a fall in metabolism accompanying recumbency or from a combination of the two factors. The removal of clothing causes new gradients to be established between the surface temperature and that inside the body, with concomitant changes in the distribution of the blood.

On examination of charts 1 and 2 it may be seen that the initial drop in the rectal temperature was considerably greater for the normal controls than for the patients, whereas in the case of the oral temperature the change was approximately the same for the two groups. In order to appreciate the meaning of this difference, the differential between the oral and the rectal temperature can be examined. The word "differential" will be used to designate the value obtained by subtracting the oral temperature from a simultaneous rectal reading. Chart 4 shows the time sequence of the means of the rectal-oral temperature differentials for patients and for normal subjects on both experimental days. These values are given in table 2. At the beginning of the constant heat day the controls had a mean differential of 0.78 F., which at the end of the observation period had decreased to 0.41 F. The patients had values of 0.42 and 0.41 F., respectively. These values, as shown by the curves, indicate that the patients maintained a relatively stable mean differential, whereas the value for the normal controls started much higher but gradually fell and approximated that for the patients during the last half of the observation period. The difference between the initial value for the patients and that for the controls is significant and corroborates similar findings by Linder and Carmichael.[7]

If in the reaction of the body to stimulation generalized blood shifts occur from internal to external tissues or vice versa, the rectal-oral temperature differential would be expected to remain constant. On the other hand, if blood shifts occur in localized vascular areas, the differ-

7. Linder, F. E., and Carmichael, H. T.: A Biometric Study of the Relation Between Oral and Rectal Temperatures in Normal and Schizophrenic Subjects, Human Biol. **7**:24 (Feb.) 1935.

ential would not remain constant. The fact that the patients maintained a stable relationship between the oral and the rectal temperature therefore implies that there was a constant relationship in the temperature or supply of blood to those areas. The findings for the normal subjects indicate that there was a variable relationship between the temperature or the supply of blood to the mouth and that to the rectum. The reaction to the stimulus which occurred in the patients seemingly was a generalized movement of blood from the various internal body cavities to the periphery. The reaction in the normal subjects differed in that the splanchnic area was more affected. This difference in response suggests a loss or an inadequate organ-selective mechanism of distribution of blood in the schizophrenic patient.

Turning to a consideration of the effect of heat, it was noted that the schizophrenic patients responded more rapidly and showed greater resultant effects. "The heat loss from the surface in the absence of sweating is mainly dependent on the difference in temperature between the skin surface temperature and the air, and the transference of heat through the subcutaneous tissue and skin is proportional to the temperature gradient, if the heat conductivity of these tissues is maintained constant." [8] If, however, as a result of vasodilatation the heat conductivity of the skin is increased, the same amount of heat may be transmitted at a lower gradient. If no vasomotor adjustment were possible, vasodilatation not occurring, the temperature of the body as a whole would rise until the requisite gradient was established. Since the increases in the body temperature of the patients were not extremely rapid, the vasomotor adjustments were not absent, but it seems that their efficiency of response was below that of the normal subjects.

It may, however, be emphasized that the environmental temperature never exceeded the body temperature, and consequently the subjects could dissipate heat from the body by any combination of evaporization, conduction and radiation. In order to throw further light on the physiologic mechanisms responsible for the differences between the controls and the patients further experiments are necessary. These experiments must present such combinations of environmental temperature and humidity as to test separately each method of heat dissipation.

SUMMARY

A method is described whereby the oral and rectal temperatures of twenty-six schizophrenic patients and sixteen normal controls were compared when the subjects were under the stimulation of an increase in the environmental temperature. All subjects were recumbent and nude when submitted for a period of three and one-half hours to each

8. Bazett, H. C.: Physiological Responses to Heat, Physiol. Rev. **7**:543, 1927.

of two different environmental conditions: one called the constant heat day, in which the room temperature was maintained at 74.3 F., and the other, the varied heat day, in which the room temperature was increased from 74.3 to 92.3 F. Oral and rectal readings were taken at half-hour intervals.

On both the constant and the varied heat days there were initial falls in both the oral and the rectal temperature. The initial drop of the rectal temperature was greater for the normal subjects. These initial falls were probably due to physiologic adjustments independent of the effect of room temperature.

On the constant heat day, near the end of the observation period there was a slight insignificant rise in the rectal temperature of the normal subjects. For the similar period there was a slight insignificant fall in the rectal temperature of the patients. On the constant heat day the oral temperature of the normal subjects increased to a terminal reading which was above the initial value. The oral temperature of the patients did not rise, but maintained a constant level.

On the varied heat day, after the initial fall, there was a subsequent rise in both the rectal and the oral temperature of the patients and of the normal controls. The rise was greater in the patients. The terminal value for the patients was significantly above the initial value. Only the terminal reading of the oral temperature for the normal controls was significantly above the initial value.

The resultant effect on the body temperature of the controlled change in room temperature and in relative humidity between the constant and the varied heat day was obtained by comparing the difference in the respective levels of body temperature. It was found that the oral and the rectal temperature of the patients increased more rapidly than did those of the normal controls.

The difference, called differential, between simultaneous readings of the oral and the rectal temperature of the patients was compared with that of the normal controls. This differential remained essentially the same for the patients throughout both the constant and the varied heat day. The differential for the normal subjects, on the other hand, began at about twice that for the patients. From the middle to the end of the observation period the differential for the normal subjects closely approximated that for the patients.

CONCLUSION

Schizophrenic subjects are unable to comply normally with the homeostatic principles concerned with the regulation of heat. Their homothermic stability seems to have been replaced by a lower phylogenetic type of adjustment mechanism, resembling poikilothermism.

ALKALI RESERVE IN BLOOD AND IN CEREBROSPINAL FLUID IN EXPERIMENTAL ACIDOSIS

E. de THURZO, M.D.*
AND
S. KATZENELBOGEN, M.D.
BALTIMORE

The object of this communication is to report the results obtained in a study of experimental acidosis in animals. The chief interest lies in investigation of the relationship between acid-base equilibrium in the blood and a similar equilibrium in the cerebrospinal fluid. The study of such a relationship, namely, of certain conditions under which artificial acidosis in the blood reflects on the acid-base balance in the cerebrospinal fluid, was inspired by bibliographic data of twofold nature: (*a*) publications of the last few years attributing great significance to acidosis in mental disorders [1] and to acidosic treatment (with a ketogenic diet) in epilepsy,[2] and (*b*) reports contending that blood substances reach and affect the nerve tissues mainly through the intermediation of the cerebrospinal fluid.[3]

TOPICS AND METHOD OF STUDY

In the light of the observations that the acid-base equilibrium of the cerebrospinal fluid is markedly more stable than the same equilibrium in the blood, we limited our investigations to two topics: 1. We studied the effect of a decrease of the alkali reserve in blood (after the injection of ammonium chloride) on the acid-base balance in the cerebrospinal fluid. Being cognizant that it takes time before changes in the content of electrolytic components in the blood show their influence on the electrolytic equilibrium in the cerebrospinal fluid, we determined the carbon dioxide-combing power in both the blood and the cerebrospinal fluid

---

* Fellow of the Rockefeller Foundation.
From the Henry Phipps Psychiatric Clinic, Johns Hopkins Hospital.

1. Mann, S. A.; Morris, R. W., and Rowe, G. K.: Studies on Acid-Base Regulation in Mental Disorders: The Determination of Urinary Acidity, J. Ment. Sc. **74**:425, 1928. Shera, G., and Cantab, B. C.: Investigation of the Acid-Base Balance in Mental Cases, with Special Reference to Epilepsy, ibid. **74**:454, 1928.

2. Talbot, F. B.: Treatment of Epilepsy, New York, The Macmillan Company, 1930. Wilkins, L.: The Present Status of Epilepsy, Internat. Clin. **2**:265, 1933.

3. Stern, L., and Gautier, R.: Les rapports entre le liquide céphalo-rachidien et la circulation sanguine, Arch. internat. de physiol. **17**:138, 1921; Les rapports entre le liquide céphalo-rachidien et les elements nerveux de l'axe cérébro-spinal, ibid. **17**:391, 1922.

at various intervals after ammonium chloride was given. 2. In order to increase the permeability of the barrier between the blood and the cerebrospinal fluid, in a certain number of experiments we combined artificial acidosis with artificial aseptic meningitis.

1. Acid intoxication was produced in cats by intraperitoneal injections of ammonium chloride (from 0.25 to 1 cc. of a 10 per cent solution), except in two cats which received the drug intramuscularly. Blood (10 cc.) and cerebrospinal fluid (from 1 to 1.5 cc.) were obtained, respectively, by cardiac and suboccipital puncture. Punctures were done before the injection of the ammonium chloride and at various intervals—from one to forty-eight hours—after the injections.

TABLE 1.—*Carbon Dioxide-Combining Power of Blood and Cerebrospinal Fluid Before and After the Injection of Ammonium Chloride*

	CO_2-Combining Power, Vol. %					
	Initial		In Acidosis		Time After Injection, Hours	Ammonium Chloride (10%), Gm.
Number	Plasma	CSF*	Plasma	CSF		
1	39	50	11	54	1	0.75
2	41	49	11	49	1	0.75
3	32	44	12	43	1	0.75
4	33	45	23	44	1	0.5
5	42	48	11	37	1	1.0
6	32	51	23	45	1	0.5
7	36	53	26	53	2.5	1.0
8	46	51	26	48	3	1.0
9	40	50	23	52	3	1.0
10	46	51	42	27	4	1.0
11	41	49	12	51	5.5	0.75
12	39	50	13	49	5.5	0.75
13	32	44	16	37	5.5	0.75
14	43	51	24	49	7	1.0
15	39	53	33	54	7	0.75
16	37	53	18	51	7	0.75
17	43	51	25	47	10	1.0
18	40	45	26	40	24	1.0
19	18	46	13	41	24	1.0
20	39	48	18	40	24	1.0
21	46	51	31	43	24	1.0
22	40	50	28	40	24	1.0
23	46	51	38	48	48	1.0
24	46	51	37	48	48	1.0
25	40	50	17	39	48	1.0

* CSF means cerebrospinal fluid.

2. From ten cats, blood (from 5 to 7 cc) was obtained by cardiac puncture and spinal fluid (from 1 to 1.5 cc.) by suboccipital puncture. Without removing the needle we immediately injected into the cisterna magna a protein preparation (from 0.2 to 0.5 cc.). From two to four hours later, ammonium chloride was injected intraperitoneally (from 8 to 10 cc. of a 10 per cent solution). Cardiac and cisternal punctures were repeated at intervals ranging from three to twenty-three and a half hours after the ammonium chloride was given. In two control experiments, that is, experiments in which meningitis was provoked but ammonium chloride was not given, the carbon dioxide-combining power was determined in the blood and cerebrospinal fluid before, and, respectively, five and twenty-four hours after, the injection of a protein preparation. Our observations in the two series of experiments were checked against those in the control experiments.

RESULTS

Only the experiments are recorded in which ammonium chloride caused a distinct decrease of the carbon dioxide-combining power in the blood plasma, regardless of whether or not the acidosis was accompanied by lowering of the carbon dioxide-combining power in the cerebrospinal fluid. In accordance with the control experiments, a difference of carbon dioxide-combining power beyond 5 volumes per cent in both blood and cerebrospinal fluid was considered to be a definite change.

1. Table 1 summarizes the results obtained in animals which were rendered acidosic in the blood and were not subjected to aseptic meningitis. The following data are shown: Of six experiments (1 to 6) in which acidosis in the blood was marked one hour after the admin-

TABLE 2.—*Acidosis and Aseptic Meningitis*

	CO_2-Combining Power, Vol. %									
	Initial		In Acidosis			Protein Preparation		Ammonium Chloride (10%)		Hours After Ammonium Chloride
No.	Plasma	CSF*	Plasma	CSF	Cells in CSF	Time	Dose, Cc.	Time	Dose, Gm.	
1	44	51	24	39	.....	12:30	0.5	4:00	1.0	18.5
2	30	48	19	34	1,400	9:30	0.5	12:00	1.0	4
3	32	50	23	27	40,000	12:30	0.5	4:15	1.0	18
4	32	49	24	34	7,300	12:30	0.5	4:15	1.0	18
5	39	49	27	41	4,900	12:30	0.5	4:15	1.0	18
6	41	52	20	36	2,000	8:45	0.5	12:15	0.8	3
7	40	..	24	31	6,000	8:45	0.5	12:15	0.8	3
8	42	39	18	33	10,000	10:30	0.25	12:30	0.8	23.5
9	40	43	32	29	1,300	10:30	0.2	12:30	0.8	3
10	32	48	12	29	.....	9:30	0.2	12:30	0.8	3.5

* CSF means cerebrospinal fluid.

istration of ammonium chloride, the carbon dioxide-combining power of the cerebrospinal fluid decreased moderately in two (5 and 6). In one (experiment 10) the mild diminution of carbon dioxide-combining power in the blood (from 46 to 42), obtained four hours after the injection of ammonium chloride, was accompanied by a significant fall of the carbon dioxide-combining power in the cerebrospinal fluid (from 51 to 27). In one experiment (13), marked acidosis in the blood obtained five and one-half hours after the administration of ammonium chloride coincided with moderate diminution of the carbon dioxide-combining power in the cerebrospinal fluid. Of five experiments (18 to 22) in which acidosis in the blood was noted twenty-four hours after the injection of ammonium chloride, the carbon dioxide-combining power in three (20, 21 and 22) also dropped in the corresponding cerebrospinal fluid. Finally, of three experiments (23, 24 and 25) in which blood and cerebrospinal fluid were withdrawn forty-eight hours

after the injection of ammonium chloride, a marked fall in the carbon dioxide-combining power of the cerebrospinal fluid was found in one (25). Thus, in only eight of twenty-five experiments was acidosis in the blood accompanied by more or less marked changes in the carbon dioxide-combining power of the cerebrospinal fluid.

2. The results obtained in the experiments in which both acidosis in the blood and aseptic meningitis were provoked are summarized in table 2. It shows that in eight of the ten cats the acidosis was accompanied by a marked drop in the carbon dioxide-combining power of the cerebrospinal fluid, and that in the two remaining animals (5 and 8) the drop was moderate. The simultaneous changes in the acid-base balance in both the blood and the cerebrospinal fluid were noted at each of the intervals, that is, three, three and a half, four, eighteen and twenty-three and a half hours after the administration of ammonium chloride. In all the experiments meningitis was pronounced, as shown by the high pleocytosis.

SUMMARY AND COMMENT

1. The first six experiments (1 to 6) showed that one hour after the administration of ammonium chloride acidosis in the blood may be pronounced.

2. The acid-base balance in the cerebrospinal fluid proved to be markedly more stable than that in the blood: Of twenty-five experiments in which acidosis in the blood was observed from one to forty-eight hours after the injection of ammonium chloride, in only eight was the carbon dioxide-combining power of the cerebrospinal fluid more or less reduced. The reduction, however, was usually mild. In seventeen experiments there was no significant drop in the carbon dioxide-combining power of the cerebrospinal fluid.

3. Of ten experiments in which both acidosis in the blood and aseptic meningitis were provoked, eight showed marked reduction and two showed mild reduction of the carbon dioxide-combining power in the cerebrospinal fluid.

4. The results of these investigations suggest that acidosis in the blood, if combined with inflammatory processes within the cerebrospinal cavity, is apt to affect the acid-base balance in the cerebrospinal fluid.

5. In the light of the previous studies of one of us (S. K.) [4] showing that there is in epileptic patients a marked tendency to high barrier permeability, one may assume that in the ketogenic treatment of such

4. Katzenelbogen, S.: The Permeability of the Hemato-Encephalic Barrier in Epilepsy, as Determined by Walter's Bromide Test, J. Nerv. & Ment. Dis. **75:** 144, 1932.

patients the acidosis in the blood induces more or less marked reduction of the carbon dioxide-combining power of the cerebrospinal fluid in many of them.

6. It would be interesting to investigate whether or not the therapeutic results obtained with the ketogenic diet in epileptic patients can be related to the permeation of acidosic substances from the blood into the cerebrospinal fluid.

7. Another topic for further investigation suggested by our results is the histologic examination of the tissues of the brain in animals in which acidosis is limited to the blood only and in those in which acidosis affects both the blood and the cerebrospinal fluid.

OBSERVATIONS FOLLOWING LEFT (DOMINANT) TEMPORAL LOBECTOMY

REPORT OF A CASE

JAMES C. FOX JR., M.D.
Associate Clinical Professor of Neurology
AND
WILLIAM J. GERMAN, M.D.
Assistant Professor of Surgery
NEW HAVEN, CONN.

Comprehensive studies of the physiologic and psychologic changes subsequent to cerebral lobectomy in man are sufficiently rare to justify reporting an individual case. This approach to the problem of cerebral localization of function has been, for obvious reasons, seldom used in the past. Its possibilities indicate the advisability of such investigations on all suitable clinical material. The present report is the result of a cooperative study of a patient following left (dominant) temporal lobectomy.

REPORT OF A CASE

History.—W. O., a white man, aged 28, entered the hospital with the chief complaint of attacks of numbness and twitching on the right side. The first symptom was a generalized convulsion, two years before admission. This was followed by occasional similar attacks at about weekly intervals and by minor seizures, occurring once or twice a day, which involved the right hand and which were preceded by numbness of the entire right side. Facial paresis gradually appeared on the right side. There had been occasional tinnitus in the left ear for two months. The patient was not aware of any speech defect except a slight difficulty in choosing words for a short time following the convulsive attacks. He had not experienced visual or olfactory hallucinations, impairment of memory, personality changes or headache. He was right-handed.

Neurologic examination revealed the following positive findings: right papilledema, 1 diopter; a slight homonymous defect of the right upper quadrant of the visual fields (fig. 1); right hemiparesis, more marked in the face and arm; hyperactive deep reflexes; diminished abdominal reflexes, and a positive Babinski sign on the right. There was no disorder of sensation or disturbance of the speech function.

At operation a large astroblastoma was identified in the anterior portion of the left temporal lobe. The lobe was resected at a point 5 cm. from the temporal pole, as measured along the sylvian vessels after the removal was completed (fig. 2).

From the Departments of Medicine and Surgery, Yale University School of Medicine.

Read at the Sixtieth Annual Meeting of the American Neurological Association, Atlantic City, N. J., June 5, 1934.

The section passed through the temporal horn of the ventricle and included the temporal portion of the island of Reil. The anterior temporal branches of the middle cerebral artery were clipped without disturbance of the parent vessel. Bits of tissue removed from the cut surface of the temporal lobe and the island of Reil later revealed the presence of a tumor in the former location. Accordingly, after

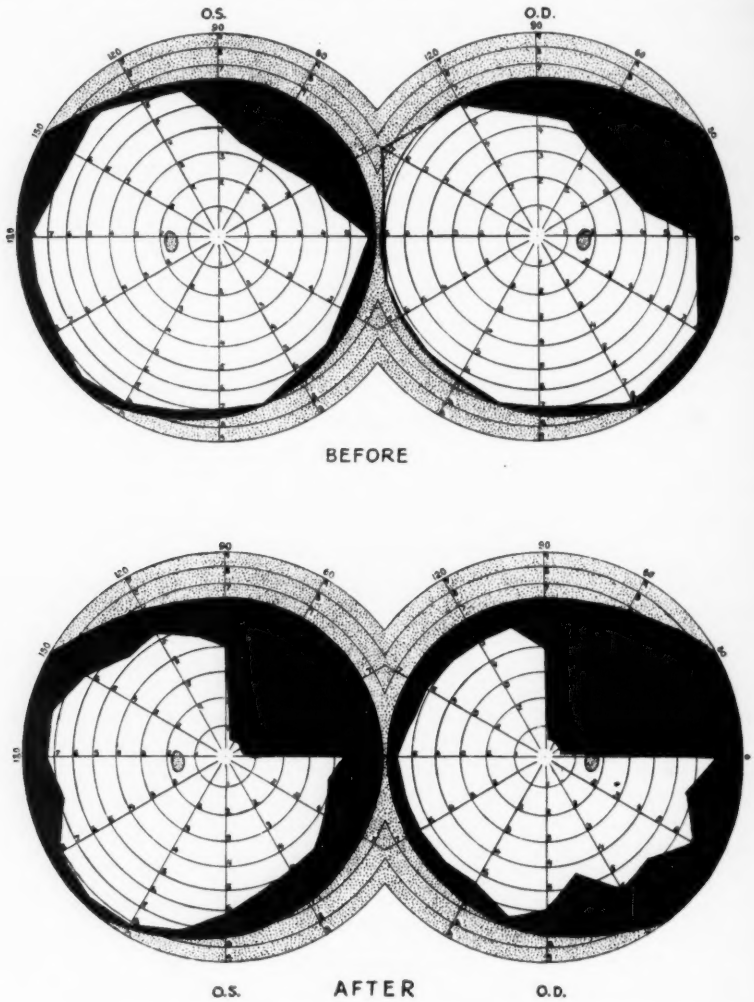


Fig. 1.—The visual fields before and after operation.

an interval of twelve days, an additional section, 2 cm. in width, was removed from the temporal lobe. After this procedure the line of resection was found to be 3 cm. posterior to the junction of the rolandic and sylvian fissures. On this occasion bits of tissue from the cut surface revealed no evidence of tumor remaining.

The portion of the temporal lobe removed included all of Brodmann's areas 20, 28, 35, 38 and 41 and the anterior portion of areas 21, 22, 36, 37 and 42 (fig. 3).

The chief association tracts involved were the uncinate fasciculus, the inferior occipitofrontal fasciculus and Meyer's loop of the optic radiations (fig. 4).

Immediately after the first operation there was pronounced aphasia, which improved rapidly during the next twelve days. Following the second operation there was a transitory increase in the aphasia. This rapidly subsided, and by the eighth postoperative day performance of the various speech tests was somewhat superior to that obtained six days after the first operation. The visual fields showed a more marked homonymous defect in the right upper quadrant after the

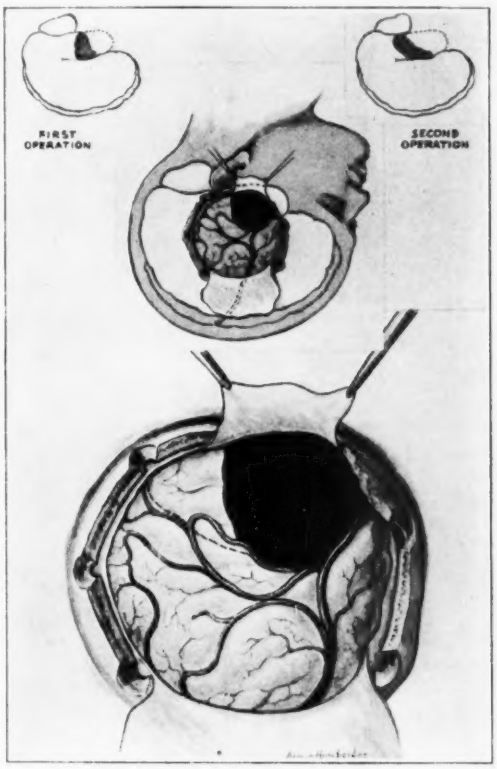


Fig. 2.—Sketch of the operative field after the first stage of the resection of the temporal lobe. The dotted lines indicate the location of the second stage of the resection.

first operation. This had encroached to within 4 degrees of the fixation point following the second operation (fig. 1). There was no change in the motor or sensory status.

An analysis of the speech function one week after the first operation revealed the following significant findings: Spontaneous speech was limited, and there was marked difficulty in finding words; the responses at times suggested a lack of orientation as to time and place. However, there was frequent inability to understand verbal questions, the patient's answers often bearing no relation to the question. Moderate verbigeration was present.

Q. Do you know where you are?
A. Oh, pretty fair. Coming back a little bit. Don't know everything though.
Q. Do you know the name of this hospital?
A. No, I don't think so.
Q. Do you know what city this is?
A. I try to—it's real hard. I'm afraid I don't know. If I wake up in a little while, I might know it.

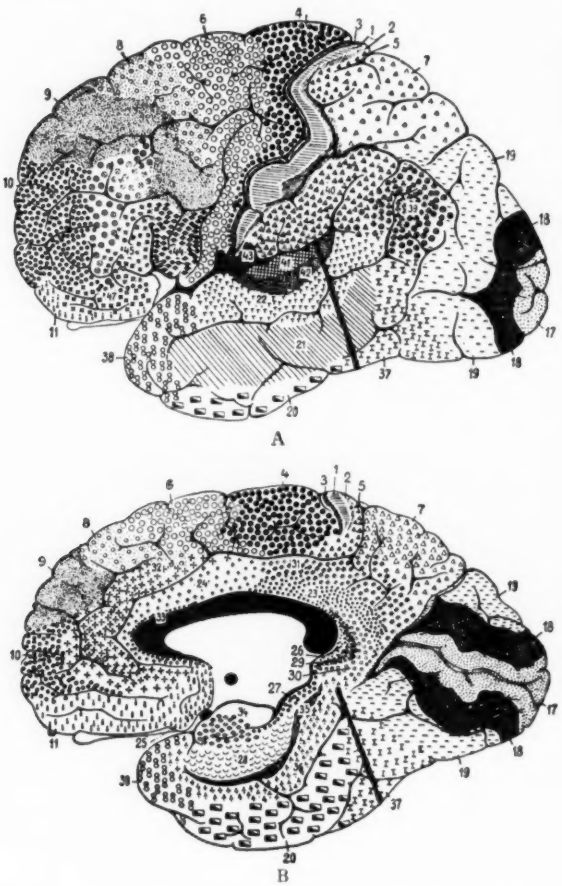


Fig. 3.—Drawings showing the relation of the resection to Brodmann's areas.

Q. Do you know what day it is? (Monday.)
A. Monday. I know that. Tomorrow will make a week that I got my first cut-upping. (Correct.)
Q. Do you know what month it is?
A. I don't know what day—is it the 9th? I came on the 3d and stayed through a day. That makes it the 23d. (Correct date.) Is that right? I got some of it back.

Q. Previous question repeated.

A. The day is almost over. About seven more days and this month will be over. The 1st of the month will end it all.

Q. Do you know what year this is? (1933.)

A. Yes. 1931. New Year.

Q. How far from home are you?

A. How far? I've been home a little over a month. Came here on Thursday. Feels good that I can tell something now; couldn't do it before.

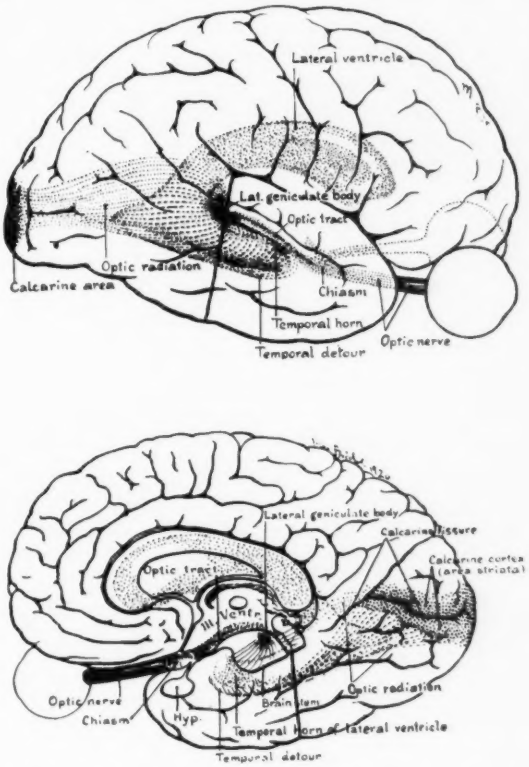


Fig. 4.—Drawings showing the relation of the resection to the optic radiation.

There was complete inability to name objects, but the correct name was usually recognized when supplied. The patient had a tendency to repeat the names of previously mentioned objects and to state or demonstrate the use of the object to be named. He was, however, able to identify correctly fourteen of fifteen objects which were named by the examiner. The tests of color recognition demonstrated a severe defect in the visual-verbal mechanism. The superiority of the visual-manual response over the auditory-manual response was also manifest.

Q. What color is this? (Green.)

A. I cant't say it—yeh—I don't know—try and say it. I can still see it. C-O-M-O-S-P-O-T-I-N. (The patient was looking at the Cosmopolitan Magazine.)

Q. Previous question repeated. (Green.)
A. It's gray. I can say it.
Q. What color is this? (Red.)
A. Red.
Q. What color is this? (Red shown again.)
A. Still the same thing. Try and say it now! (Laughed.)
Q. What color is this? (Blue.)
A. Gray, I—yeh, that's gray sure.
Q. What color is this? (Yellow.)
A. Yeh—I know what it is. Gee, try and think—gee, I ought to know that. Try and think of it; I give up.
Q. Point to the red. (Verbal command.)
A. That's gray. (But he pointed to the red.)
Q. Point to the blue. (Verbal command.)
A. (Correct response.)
Q. Point to the yellow. (Verbal command.)
A. (No response.)
Q. Point to the yellow. (Written command.)
A. (Correct response.)
Q. Point to the red. (Verbal command.)
A. (No response.) I can with the writing.
Q. Point to the red. (Written command.)
A. (Correct response.)

Reading aloud was limited to a few simple words. The significance of pictures was appreciated, but attempts to describe them revealed agrammatism and difficulty in naming objects. The patient occasionally resorted to spelling out a word he could not say.

Q. What is the significance of this? (The patient was shown an advertisement for Lucky Strike cigarets, depicting a man blowing a smoke ring about a woman's ring finger.)
A. Man and woman—strike—just going to say it—strike—couldn't get it. Man and a woman—he's already given her—she's already engaged to be married; she and the boy-friend. Advertisement for Lucky Strikes. He's smoking a Lucky Strike.
Q. Lucky Strike what? What is he smoking?
A. Lucky Strike cigaret.
Q. What is he wearing?
A. He's got—I don't what you call it—I can't say it. I give up there.
Q. Read this. (Legend under advertisement.)
A. Forever and ever (hesitation). It's toasted. (Correct.)

Writing his name and address on verbal command revealed a slight tendency to repetition. Writing to dictation was incorrectly done, though definite words were formed. Copying was accurately done. The patient was unable to write the Lord's prayer but recited the first and third lines correctly, at the same time writing something which he had previously seen in the reading test (fig. 5). Recitation of the Lord's prayer was limited to the same two lines. In response to a written command the patient was able to write the alphabet as far as "u" and recited the remainder correctly. The written letters showed three mistakes in twenty-one attempts. Drawing to verbal command revealed four mistakes in five attempts. Copying, drawing to written command and drawing from memory were well done. Sounds were accurately recognized and localized, but the patient's

response showed a paucity of names and a tendency to spell the name or paraphrase it by giving the action performed. There was no evidence of apraxia.

Ten days after the second operation spontaneous speech was considerably improved. Questions were more readily understood, and orientation to time and place was fairly accurate. The tendency to spell out proper names persisted, but verbigeration was less marked. The patient was unable to name any of the test objects but indicated their use or association with other objects. The ability to identify objects named by the examiner remained essentially the same. Reading aloud was improved, but there was a tendency to omit, add, change or mispronounce some words. The patient wrote his name and address correctly to verbal

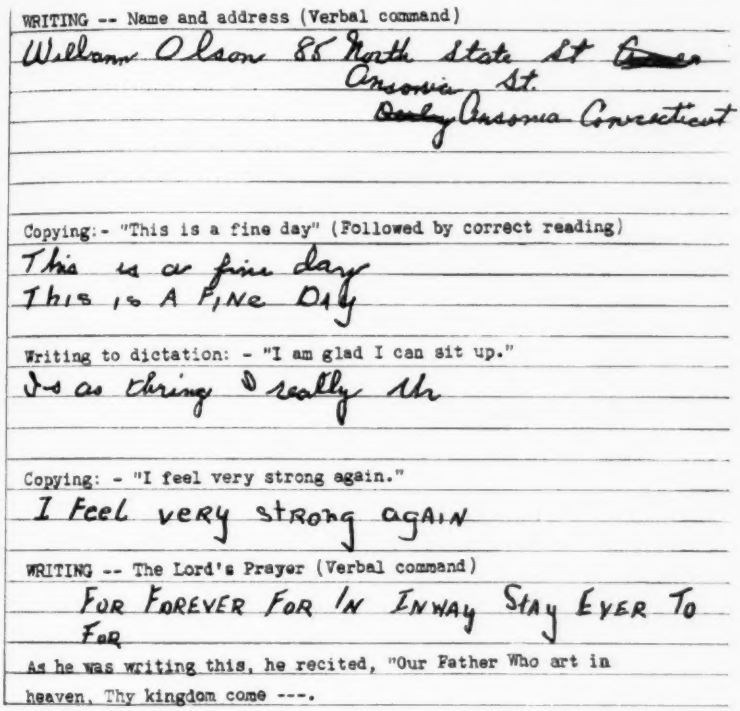

WRITING -- Name and address (Verbal command)
William Olson 85 North State St
Ansonia St.
Derby Ansonia Connecticut
Copying:- "This is a fine day" (Followed by correct reading)
This is a fine day
This is A Fine Day
Writing to dictation: - "I am glad I can sit up."
I-s as thing I really th
Copying: - "I feel very strong again."
I Feel very strong again
WRITING -- The Lord's Prayer (Verbal command)
For Forever For In Inway Stay Ever To
For
As he was writing this, he recited, "Our Father Who art in
heaven, Thy kingdom come ---.

Fig. 5.—The patient's writing six days after the first operation.

command, but writing to dictation was defective (fig. 6). Drawing to verbal command was improved. The practical response was more accurate when commands were written than when they were spoken.

Recovery of speech function took place rapidly at first and then more slowly. During the first year after operation the patient noticed considerable difficulty in attempting to follow several conversations at one time. When he was listening to speeches on the radio he could understand everything that was said during the first few minutes. After that the words seemed to become "jumbled" and all continuity was lost. Essentially, the same difficulty was experienced when he was reading. He would progress fairly satisfactorily for the first few paragraphs. Then he would begin to miss the meaning of some words, and the mistakes would multiply

rapidly. Finally, as the patient explained it, his "mind became so full of words" that he lost the significance of what he was reading and was compelled to stop.

During the thirteenth postoperative month a moderately intensive course of reeducation was begun. Examples of the patient's writing to dictation at the beginning of this period showed a defective auditory receptive mechanism (fig. 7). His training progressed, and a month later performance showed definite improvement (fig. 8). Spontaneous speech was free, intelligible and of normal frequency, with an occasional slurring of words and a relatively limited vocabulary. Pronunciation was usually correct, with no tendency to misplace words or syllables. Tactile and visual perception were normal, but there was definite difficulty in naming objects. Reading aloud was particularly difficult, and there was a tendency to spell out certain words, although the same word might be used spontaneously in conversation at another time. Thus he spelled out "electric" at one time, although before and after this he used the same word spontaneously in conversa-

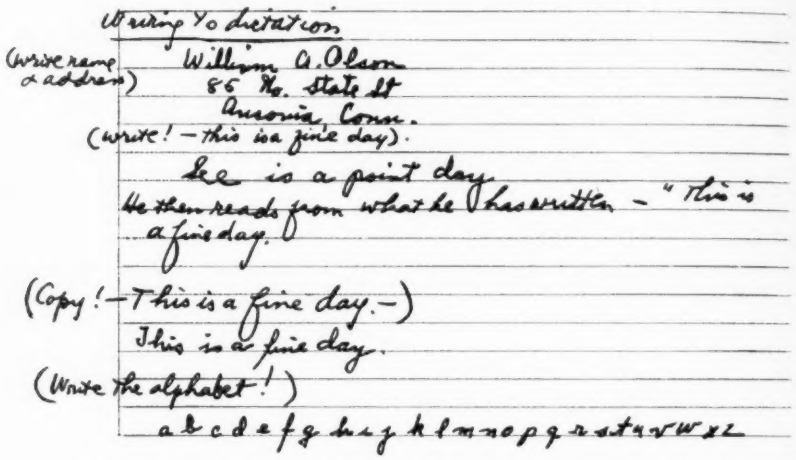

Writing to dictation
(Write name & address)
William A. Olsen
86 No. State St
Ansonia, Conn.
(write! – this is a fine day).
See is a point day
He then reads from what he has written – "This is a fine day.
(Copy! – This is a fine day. –)
This is a fine day.
(Write the alphabet!)
a b c d e f g h i j k l m n o p q r s t u v w x z

Fig. 6.—The patient's writing ten days after the second operation.

tion. This is particularly interesting because he formerly worked for the General Electric Company. Auditory perception still showed a defect in interpreting complicated verbal commands. This difficulty was absent when the commands were presented in written form. Writing was accurately performed, but the difficulty in recalling specific words was the same as in reading aloud. Copying showed no errors. The practical response was normal except for occasional hesitation and apparent confusion in interpreting commands. Music was appreciated and enjoyed. Familiar tunes were recognized and occasionally sung by the patient. Retention of auditory material was definitely inferior to that of visual experience. The patient was unable to repeat a series of more than two unrelated words or numbers. However, when the numbers were presented in graphic form he was able to reproduce in writing series of four numbers of two digits.

Psychologic determinations were made on the patient by Dr. Walter Miles at intervals after the operation. Intelligence ratings, based on two picture completion tests (Healy tests 1 and 2) involving no verbal activity, indicated average intelligence. Cooperation was excellent, and the patient was willing to attempt any task assigned to him. The reaction time on both sides was within normal

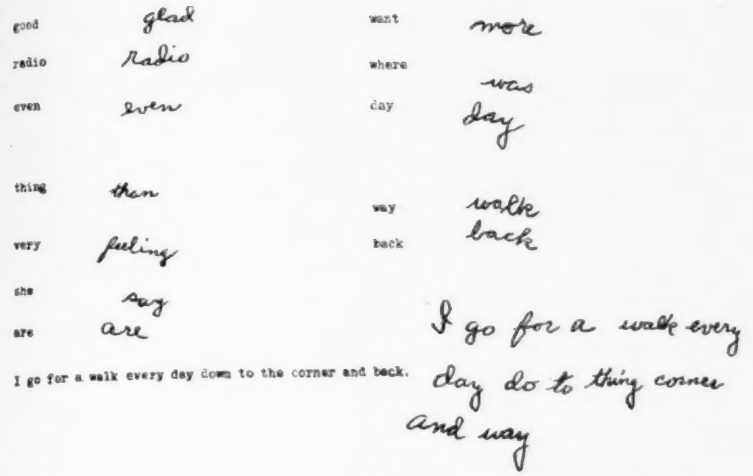


Fig. 7.—The patient's writing to dictation thirteen months after the operation.

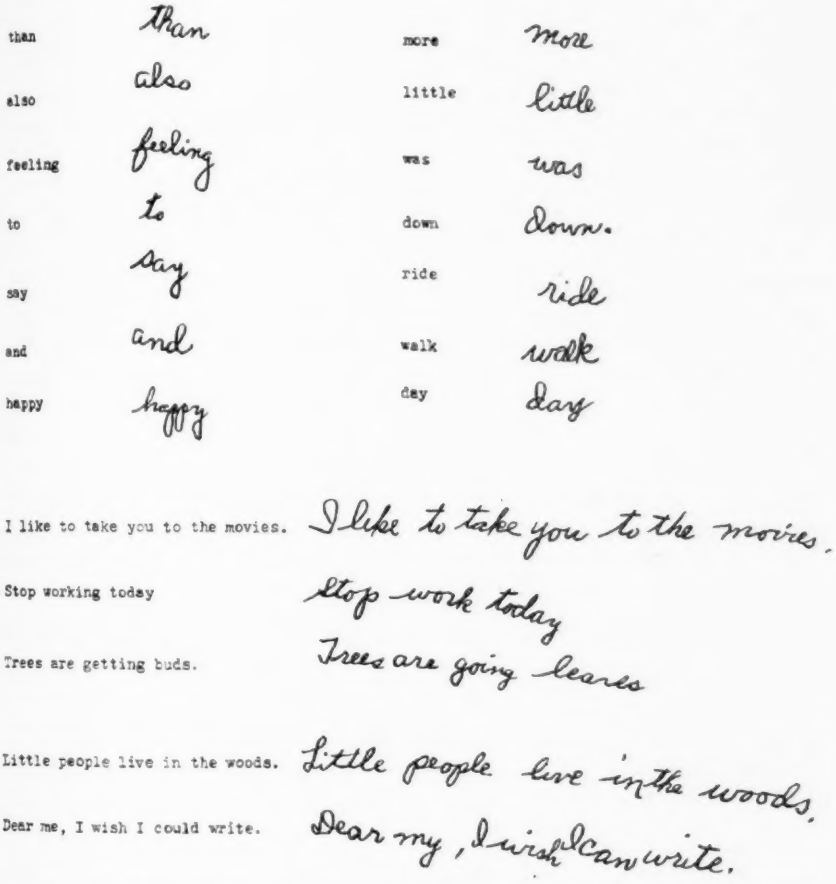


Fig. 8.—The patient's writing to dictation fourteen months after the operation and at the end of one month of intensive reeducation.

limits. He exhibited dominance of the right eye but not of extreme degree. There was no evidence of spatial disorganization.

Present Intellectual Status.—Fifteen months after operation the intelligence quotient was from 100 to 118; on the basis of the Healy picture completion tests 1 and 2, the cube completion test, the Ferguson form boards (all six), parts of the army beta tests and the nonlanguage parts of other tests, the mental age was about 16. Language difficulty and lack of speed accounted for the chief decrement. Making allowance for these, the probable intelligence quotient was 120. There was no decrement in the ability to make use of recent experiences in terms of memory. Performance was smooth and well considered, of adult type. Attention was not narrow and showed no defect; the point of view was easily changed. There was probably a slight increase in suggestibility. Perceptual capacity in the visual field appeared normal. Mathematical ability was about 25 per cent below the average. There was some evidence of preference for the left hand in the tests of performance, but the dominance of the right hand remained unchanged.

Eye Movements.—Photographic records of the movements of the eyes were obtained three days before the first operation, seven days after the first operation and fourteen days after the second operation. The Dodge mirror recorder was used. This technic employed the principle of photographing horizontal conjugate deviations of a closed eye. Four different optical situations were studied: (1) pursuit of a pendulum, (2) optokinetic nystagmus, (3) response to commands to look to the right and left and (4) response to peripheral retinal stimulation. With the exception of a slight increase in the corrective refixation movements appearing in all of the records, the ocular response was found to be normal in every respect. However, it should be added that under the experimental conditions employed, in the static and moving visual fields, at no time was the visual stimulus actually within the blind quadrant.

Personality.—The patient entered college at the age of 17, where he made many friends but could not afford to join a fraternity. He engaged in athletics (tennis and swimming) but did not make a team. He stood fairly well in his studies but withdrew from college at the end of the second year because his finances did not provide the scale of living which he demanded. He held several clerical positions, the last one being with the General Electric Company. He was considered to be a hard worker and ambitious, perhaps beyond his capabilities. For several years before the onset of the illness and for a considerable time during its early course he was engaged to be married. The match had been discouraged when it was understood that he was subject to epilepsy. He was always genial and jovial, had no significant swings of mood, was only rarely irritable and, like his twin sister, "could always make a joke out of everything." This was true even shortly before the operation, after it had become necessary for him to stop working.

There appeared to be no striking change in the patient's personality after the operation. He continued to be jovial; he enjoyed company and was popular with his friends. He was content to spend most of his time quietly at home. He took short walks and occasionally went to the movies or attended informal social functions. His activities were normally spontaneous and purposeful. A girl of about his age came to see him frequently. During the thirteenth month after the operation she began to teach him to read and write. He appeared to be genuinely fond of her and grateful for her assistance. His attitude toward the opposite sex did not appear to change. He appeared to be anxious to regain his ability to read, write and speak normally in order to "get back on the job," but he did not chafe at the long unemployment which his illness necessitated. He was just as meticulous

in dress and manners as before. There were no impulsive outbursts of temper. During the illness and for a considerable period after operation he was afraid to meet people or to be in a crowd. This tendency disappeared.

There appeared to be some emotional instability. On meeting visitors he laughed a little more excitedly than one would expect for a normally poised man of his age. However, he soon became calm and extremely congenial. There was frequent recurrence of the same sort of poorly controlled laughter whenever he became aware of a speech difficulty. He was not facetious. He enjoyed talking but did not resent being interrupted. When this occurred, he took up the conversation where it left off and finished his story.

COMMENT

Is there justification for drawing conclusions regarding functional localization from "experiments" of this type? Penfield and Evans [1] aptly stated that "the ideal manner of studying the music produced by a violin was not analysis of a symphony orchestra after that instrument had been removed." However, it is equally obvious that one cannot study a cerebral "violin" by removing the remainder of the "orchestra." Stimulation experiments are obviously applicable to only the grosser forms of motor and sensory functions. The correlation between a disturbance of cerebral function during life and a structural defect found post mortem has always been handicapped by the nondiscrete and progressive nature of most neoplastic and vascular lesions. Careful serial studies following cerebral lobectomy constitute a valuable and until recently unexplored method of study of cerebral function.

There are certain objections to this method. Slowly growing tumors tend to displace the surrounding tissue. A considerable portion of the brain tissue removed has already been rendered functionally abnormal. It appears likely that functional restitution has already proceeded coincident with the cerebral destruction, prior to lobectomy. Consequently, only in cases of relatively small, infiltrative tumors in which destruction of the tissues has been minimal does this method of study seem most applicable. Another objection which immediately comes to mind is the interruption of hemispheral pathways by the transection. The "center" effect is, of course, only part of the disturbance of function which may result. The necessity for this differentiation is illustrated in the present case by the defect of the visual field, which obviously can be ascribed only to a lesion of a tract.

Hughlings Jackson said that destruction of cerebral tissue has two effects: (1) the abolition of the specific function of the tissue removed and (2) the unleashing effect on lower, subservient centers. It would be unwise to ascribe the euphoria which the patient exhibited directly

1. Penfield, W., and Evans, J.: Functional Defects Produced by Cerebral Lobectomies, Proc. A. Research Nerv. & Ment. Dis. **13**:352, 1934.

to the loss of the major portion of the left temporal lobe. The same symptom appeared in our patients following frontal and occipital lobectomies.[2] This might be accounted for by Jackson's release mechanism. If these two effects of such a "negative" lesion, as well as the possibilities of functional restitution, are borne in mind, lobectomy occupies a legitimate place in the study of cerebral localization.

Speech.—Applying these facts to the aphasia resulting in this case, one is immediately confronted with the difficult problem of speech analysis. Head [3] stated that neither the areas of localization nor the resulting loss of function determines the "elements out of which language is composed" but the manner in which "the use of language can be broken up." Weisenburg,[4] after the most comprehensive clinicopsychologic attack ever made on the problem of aphasia, stated: "I have come to the conclusion that it is not possible definitely to localize aphasic disturbances." The frequent association of certain symptoms, such as the inability to name objects, with widely divergent lesions suggests that such is the case. However, an appreciation of the diverse afferent pathways, visual, auditory, tactile, even olfactory and gustatory, through which such specific mental associates are established, transforms this apparent paradox into a logical result. It is only through analysis of the various receptive, associative and expressive components of the speech function that specific defects may be identified in the present case. It then becomes evident that the auditory receptive mechanism is most deficient. A defect in the retention of auditory speech memories is likewise notable. Although language, as an intellectual faculty is not capable of such localization, it is obvious that, in the present case at least, the auditory component of the speech mechanism is related to the dominant temporal lobe. This conception is compatible with Henschen's [5] view.

Vision.—The defect of the upper quadrants of the visual fields and the location of the resection are in accord with Meyer's [6] description of the temporal loop of the optic radiation which bears his name. The course of the geniculocalcarine fibers through the temporal lobe led

2. German, W. J., and Fox, J. C.: Observations Following Unilateral Lobectomies, A. Research Nerv. & Ment. Dis., Proc. **13**:378, 1934.

3. Head, H.: Aphasia and Kindred Disorders of Speech, Brain **43**:87, 1920. Speech and Cerebral Localization, ibid. **46**:355, 1923.

4. Weisenburg, T. H.: A Study of Aphasia, Arch. Neurol. & Psychiat. **31**:1 (Jan.) 1934.

5. Henschen, S. E.: Clinical and Anatomical Contributions on Brain Pathology, pts. 5, 6 and 7, abstracted and commented on by W. F. Shaller: Arch. Neurol. & Psychiat. **13**:226 (Feb.) 1925.

6. Meyer, Adolf: The Connections of the Occipital Lobes and the Present Status of the Cerebral Visual Affections, Tr. A. Am. Physicians **22**:7, 1907.

Cushing [7] to investigate the visual fields in cases of tumor of the temporal lobe. The frequent preservation of macular vision, even in the presence of an otherwise complete homonymous hemianopia, is a striking feature in Cushing's cases. Brouwer's [8] studies on the retinal projection in the external geniculate body and the calcarine area [9] indicate an extensive macular representation. It appears likely, therefore, that the macula is diffusely represented in the optic radiation as well. Such a hypothesis most readily explains the macular preservation in the present case and also suggests that half of the macular vision is lost only when the entire optic radiation is involved. In the light of Poljak's [10] recent findings it seems unnecessary to consider the possibility of bilateral macular representation (Heine [11]).

Personality.—The personality, considered in terms of its specific components—physical characteristics, impulse, temperament and character—suffered little change as a result of the resection of the temporal lobe. The patient had always been a rather active man of slight build, not disposed to frequent illnesses. The only change in this respect after operation, was a gain of 20 pounds [9.1 Kg.] in weight. The patient appeared to be of average intelligence, and, with the exception of the speech difficulty, no intellectual defect resulted. Prior to operation he had been ambitious, perhaps beyond his capabilities. A reduction in drive was suggested by his attitude of resignation toward the illness. He had always been of a jovial, outgoing temperament, but this characteristic increased to the extent of definite euphoria after the operation. New situations induced a degree of emotional instability, but adaptation was rapid. His personal habits and social attitudes remained unchanged, and there was no lack of normal restraint.

Restitution of Function.—Probably the most striking feature of this case, and one that was likewise prominent in the cases of lobectomy previously reported,[8] was the degree of functional restitution. It is difficult to evaluate the significance of this recovery. Does it indicate that cerebral function is dependent chiefly on cerebral mass (Lash-

7. Cushing, Harvey: Distortions of the Visual Fields in Cases of Brain Tumor: The Field Defects Produced by Temporal Lobe Lesions, Brain **44**:341, 1921.

8. Brouwer, B.: The Projection of the Retina in the Brain, Lecture on the Hertler Foundation, 1926, Baltimore, Williams & Wilkins Company, 1927, vol. 17, p. 1.

9. Brouwer, B.: Projection of the Retina on the Cortex in Man, A. Research Nerv. & Ment. Dis., Proc. **13**:529, 1934.

10. Poljak, S.: Projection of the Retina upon the Cerebral Cortex, Based upon Experiments with Monkeys, A. Research Nerv. & Ment. Dis., Proc. **13**:535, 1934.

11. Heine, L.: Sehschärfe und Tiefenwahrnehmung, Arch. f. Ophth. **51**:146, 1900.

ley [12]); that the excised portion bears only a quantitative relation to the cerebral function? The specificity of the defect, even after restitution was well established, makes this hypothesis untenable. Analysis of the functional recovery shows two distinct phases: an early, rapid improvement during the first few weeks after operation, and a later, slowly progressive phase, apparently associated with reeducation. The former is probably related to the subsidence of edema and vascular changes in the contiguous portions of the brain, the latter to actual restitution of function by other parts. Whether the functions are taken over by adjacent areas or by similar areas in the opposite hemisphere, as suggested by the case of Lowell, Waggoner and Kahn,[13] is entirely a matter of speculation. However, it is impossible to determine in any instance how much the nondominant hemisphere may have been cofunctioning prior to an injury to the brain. The only conclusion justified is that new domains of integration are established.

SUMMARY

The left temporal lobe of a right-handed man was resected 3 cm. posterior to the junction of the rolandic and sylvian fissures for removal of an astroblastoma. Speech, vision, personality and restitution of function have been studied in this patient.

Analysis of the speech involvement revealed a deficient auditory receptive mechanism and impaired retention of auditory speech memories. In contrast to this, the visual mechanism suffered a relatively slight defect. It is concluded that the auditory component of speech is related to the dominant temporal lobe.

The visual fields revealed an upper quadrantic homonymous defect with the preservation of macular vision. An extensive macular representation in the optic radiation, similar to that found in the external geniculate body and calcarine area, is suggested.

The principal personality changes were euphoria, some degree of emotional instability and slight reduction in drive.

Functional recovery demonstrated two distinct phases: early, rapid improvement, probably related to edema and vascular changes produced by the operation, and later a slowly progressive phase, apparently associated with reeducation, representing true restitution. The latter type of recovery indicates the establishment of new domains of integration.

12. Lashley, K. S.: Brain Mechanisms and Intelligence, Chicago, University of Chicago Press, 1929.

13. Lowell, H. W.; Waggoner, R. W., and Kahn, E. A.: Critical Study of a Case of Aphasia, Arch. Neurol. & Psychiat. **28**:1178 (Nov.) 1932.

DISCUSSION

DR. R. M. BRICKNER, New York: I have followed the previous and the present investigations of Dr. Fox and Dr. German on lobectomy with great interest. Their contributions have shown to a considerable degree that studies after lobectomy constitute a valuable method of examining cerebral function.

Of the many subjects suggested by them for discussion I have chosen two main topics—the effects of the removal of brain tissue on personality and the question of the vicarious restitution of function.

In the case under discussion removal of a large part of one temporal lobe had only a minor effect on the patient's personality. The most pronounced change, evidently, was the incidence of euphoria. I think that it is not surprising that the alterations were minimal, because the weight of general evidence indicates that both sides of the brain must be involved before profound changes in personality occur. This is clearly suggested in the case of the frontal lobes, and it probably holds for the other parts as well. This thesis is probably not susceptible of final proof, but a study of cases of injuries and tumors and of such cases reported in the literature supports it. This should not be understood as meaning that the cortex acts as a whole. It can be interpreted more satisfactorily in another way, namely, that the multitudinous processes aggregation of which results in what is called personality are bilaterally represented in the cortex.

What are the things which seem to have this bilateral representation? For the sake of a working hypothesis, it seems reasonable to think of them as separate, engrammic processes made up from the synthesis of many relatively simple sensory units. For the manifestation of "personality," these engrams must be able to combine freely and in many different ways—a function which may be tentatively attributed to the cortex without too great a stretch of the imagination. Whenever a certain amount of cortical tissue is lost, a certain amount of aggregative, or synthesizing, capacity goes with it, but if the loss is limited to one side of the brain the "twin set" on the other side can still take care of the necessary aggregations with moderate adequacy. If this were true, it would not be astonishing that after unilateral lobectomy fatigue should set in more promptly than normally, since one side would be acting unaided by its accustomed fellow. Sustained effort might then result in the appearance of symptoms.

This is exactly what happened in the case in question in the domain of auditory comprehension. In the first few minutes of listening to radio speeches, everything was clear, but soon the words became a jumble.

The question of vicarious taking over of function by other parts of the brain is a difficult one to consider. There is practically no real evidence which indicates whether this can or cannot happen. Most authors have not shown the restraint of Dr. German and Dr. Fox and have simply taken sides. It may be reasonable to consider this matter also from the standpoint of bilateral representation of cortical function. Possibly the so-called "vicarious functioning of the parts" represents only the capacity of the "twin cortex" to perform its activities alone with progessively less fatigue. In the only case I know of in which bilateral lobectomy (of the frontal lobes) was followed by study, there has been no apparent restitution of function of real degree in the five years since the operation. In that case, of course, no "twin cortex" was left.

One point which is especially difficult to understand from the point of view of vicarious function is the disappearance of psychic symptoms after mere decompression, when the symptoms are quite clearly not of a type which can justly be attributed to a general increase in intracranial pressure. Such recoveries can hardly

be assigned to vicarious restitution. This point has received considerable attention —notably by Puusepp. A more satisfactory hypothesis might be the reduction of direct pressure by a tumor on a relatively uninvolved opposite hemisphere.

I should like to ask the authors two questions: Was the patient's resignation toward his illness of a more or less "normal" degree, or was it too great, as it so often seems to be in cases of hemispheral injuries? Also, how real a diminution in initiative was there?

Dr. J. C. Fox, New Haven, Conn.: In reply to Dr. Brickner's question, we were unable in the limited time for presentation of the paper to go into the question of personality in great detail. The patient showed definite resignation toward his illness. When he first came to the clinic he was greatly disturbed by the fact that he had to give up his clerical position in the General Electric Company. However, since the lobectomy he has been entirely resigned to the situation. He has evidenced a desire to return to work and a feeling that eventually he will return to work, but he is not actively worried about it.

As to the lack of initiative, I should say that we must be cautious in this respect and compare his present initiative with what we know about his initiative prior to the operation. Briefly, before his illness he had shown at certain times a lack of initiative in spite of his jovial, outgoing, friendly personality. For example, he had given up college after two years because his finances were not adequate to permit the sort of life he wanted rather than doing what many men do—press on and finish their career. This was long before his illness.

We wish to emphasize one or two other points about the case. First, the members will recall that the macula was spared in the presence of an otherwise complete defect of the quadrant. We feel that this is evidence of a diffuse representation of the macula in the optic radiation and is in keeping with the conception advanced by Brouwer and confirmed, we believe, by the work of Poliak that the macular fibers have a relatively diffuse representation in the geniculate body and calcarine cortex. The question of macular involvement depends on whether or not all of the calcarine cortex is destroyed or all of the optic radiation is interrupted. We feel that in this case only the loop described first by Dr. Meyer was resected and that thereby macular vision was spared.

We also present this case not as direct evidence of localization of speech function in the temporal lobe but as an indication that the auditory receptive mechanism was markedly impaired and that there has been a marked recovery of this function.

I had the opportunity of discussing this with Dr. Weisenburg today. Unfortunately, he could not be here, but he agreed that this case would fall into his receptive group, one of the four groups described last year in his lecture on aphasia. We are willing to go a little further and say that this condition was a specific type of receptive disorder, involving primarily, and almost exclusively in the later stages, the auditory receptive phase. In that respect the case tends to confirm the views of Henschen concerning the localization of auditory speech in the part of the temporal lobe which was affected in the lobectomy.

A final point to which we should like to call attention is the possibility of lobectomy as an approach to certain problems of cerebral localization. Particularly with a detailed study of a case of this type, it appears that the method justifies further exploitation.

PHYLOGENETIC INTERPRETATION OF THE FUNCTIONS OF THE VISUAL CORTEX

DONALD G. MARQUIS, PH.D.
NEW HAVEN, CONN.

Two aspects of the problem of localization of function in the brain have always commanded the attention of neurologic investigators. These may be called, for convenience, the horizontal localization—the geography of functions in any one neural level, such as the cortex—and the vertical localization—the contribution of successive neural levels to the function in question. With respect to visual function, the problems of horizontal localization are the problems of identifying the regions of the brain concerned with vision and of analyzing the spatial relations within such regions. Recently great advances have been made in the clinical and anatomic study of the projection of the retina on the primary optic centers, the visual radiation and the calcarine area of the cortex. Few problems remain on which all investigators do not essentially agree.

No adequate answer, however, can be found for the problem of the levels of function within the visual system. From a consideration of the synaptic interruptions of the optic pathway it is apparent that there are at least three levels of integration: a subcortical center (superior colliculus), a cortical receptive center (area striata) and a cortical center of correlation (fields 18 and 19 of Brodmann). The relation between the subcortical and the cortical functions is the subject of this report. After certain obvious differences in cortical and subcortical relations between the visual system and the somatic sensory system are pointed out, an interpretation of these differences in the light of the evolutionary development of cortical function will be presented.

The facts in the case of the human visual system are clear. Clinical observations afford direct evidence that vision at a subcortical level is impossible. Destructive lesions of the area striata abolish all visual sensitivity, even the crudest perception of light and dark. Small isolated lesions result in correspondingly small scotomas; destruction of the calcarine cortex of one hemisphere causes homonymous hemianopia; bilateral destruction, total blindness. But in each instance the blindness is absolute for the region of the visual fields concerned. The pupillary

---

From the Department of Psychology and the Section of Neuro-Anatomy, Yale University School of Medicine.

Read as part of a symposium on the functions of the cerebral cortex before the Section on Nervous and Mental Diseases at the Eighty-Fifth Annual Meeting of the American Medical Association, Cleveland, June 14, 1934.

reflex remains the only response to light which is mediated by subcortical centers.

This relation between cortical and subcortical functions, however, is not true of all the afferent systems. The cerebral organization of somatic sensitivity is in marked contrast to that of vision. Following the work of Head and his collaborators [1] it has been repeatedly demonstrated that after destruction of the sensory projection fibers to the postcentral cortex there remains a primitive awareness of cutaneous stimuli presumably mediated by thalamic centers. Discrimination of fine differences in intensity, localization of stimuli and perception of size, shape and texture of objects are impaired, but the patient can still feel contact, pain, warmth and cold.

This subcortical sensitivity for somatic stimulation stands in distinct contrast to the absence of any subcortical sensitivity for visual stimulation and presents a challenging problem. I believe that it is a problem which can be clarified by a consideration of the evolution of the brain. It has long been recognized in comparative anatomy that the central nervous system shows an orderly and progressive development in the phylogenetic series, characterized by the shifting of functions from lower to higher centers and by the increasing dominance of the higher centers in the control of activity. This principle of encephalization was first systematically studied in the sphere of motor function. In a series of animals ranging from the lower mammals to primates and to man electrical stimulation of the cortex reveals an increasing number and discreteness of motor points, while the paralysis consequent on extirpation of the motor cortex is progressively more complete and permanent.

With the results of experiments on the effects of removal of the visual cortex in dogs and monkeys, it is now possible to trace the steps in the encephalization of one of the afferent functions—vision. Five stages—inframammalian vertebrates, rodents, the dog, the monkey and man—will be considered for the purpose of comparing the degree of residual function following removal of the cortical visual center.

EFFECTS OF REMOVAL OF THE VISUAL CORTEX

Inframammalian Vertebrates.—In the lower vertebrates (fish and amphibia) the chief visual correlation center is the optic tectum, the homolog of the mammalian superior colliculus. There are no optic connections to the forebrain, and removal of the cerebral hemispheres produces, therefore, no impairment of vision. The functions of the tectum are well developed, for it is known that many species of fish possess good vision for form and color.

---

1. Head, H.: Studies in Neurology, New York, Oxford University Press, 1930, vol. 2.

In reptiles and birds there is a beginning of a cerebral visual system in the projection of a small tract from the lateral geniculate nucleus to the epistriatum. The tectum, however, remains the principal visual center, and complete removal of the forebrain results in almost no visual defect.[2]

Rodents.—With the appearance of true neocortex in mammals, the central visual system undergoes a striking reorganization. Relatively many more optic fibers terminate in the lateral geniculate body, where the optic radiation arises to course to the visual cortex. The superior colliculus is smaller than the tectum of lower animals and receives a smaller proportion of the fibers of the optic tract. Throughout the mammalian series there is a progressive increase in the size of the geniculocortical system at the expense of the superior colliculus.

In rabbits the complete destruction of the visual cortex produces marked impairment of vision, but the perception of the relative brightness and position of objects is sufficiently retained to enable the animals to avoid obstacles, to jump, to climb and to recognize their food plates by sight.[3] The extensive, carefully controlled researches of Lashley[4] have demonstrated that bilateral destruction of the occipital cortex in rats permanently abolishes vision for form and pattern but that the animals retain the ability to discriminate between light and dark and to judge the position and distance of an object well enough to jump from one platform to another.

Dogs.—On the basis of the early work of Munk and Minkowski, it has generally been accepted that a dog is completely blind after the visual cortex is removed. However, it has recently been demonstrated that a sensitivity to differences in intensity of light is retained after complete bilateral removal of the occipital lobe. Some of the results of these experiments have been reported previously.[5]

The visual cortex was removed in a one stage bilateral occipital lobectomy.[6] Following the operation the dog appeared totally and permanently blind. The animal bumped into the walls of the kennel and into objects placed in its path; it did not respond in any way to food

2. Schrader, M. E. G.: Zur Physiologie des Vögelgehirns, Arch. f. d. ges. Physiol. **44**:175, 1889. Gemelli, A., and Pastori, G.: Sulla rieducabilità di animale scerebrati, Pubbl. Univ. Cattol. d. S. Cuore **6**:565, 1931.

3. Ten Cate, J., and Van Herk, A. W. H.: Beobachtungen an Kaninchen nach Exstirpationen im Neopallium, Arch. néerl. de physiol. **18**:337, 1934.

4. Lashley, K. S.: The Mechanism of Vision: II. The Cerebral Areas Necessary for Pattern Vision in the Rat, J. Comp. Neurol. **53**:419, 1931.

5. Marquis, D. G.: Effects of Removal of the Visual Cortex in Mammals with Observations on the Retention of Light Discrimination in Dogs, A. Research Nerv. & Ment. Dis., Proc. **13**:558, 1934.

6. The operations were performed by Dr. J. F. Fulton in the Laboratories of Physiology, Yale University School of Medicine.

held or moved before its eyes, and it did not blink or flinch to threatening gestures. It moved about very cautiously and slowly, with its head lowered to the floor, refusing to jump from the edge of a stool or to descend stairs unless it could explore the next step with its nose or forepaw. It appeared as fully incapacitated as a dog which had been blinded by the destruction of the retinas.

However, by training the dog to make some differential response to varying intensities of light it is possible to demonstrate that sensitivity to light is retained in such an animal with little impairment. Two methods of training have been used with mutually confirmatory results. According to the first method the dog was placed in a chamber from which there were two exit doorways. The relative illumination of the doorways could be changed, and the dog was taught to go through the more dimly lighted exit, no matter whether it was on the left or on the right. Normal dogs learn this discrimination to a criterion of thirty errorless trials after one hundred and sixty trials.

Dogs without occipital lobes were able to acquire this habit perfectly, but their progress was somewhat slower than that of normal dogs. When the habit was learned before operation it was abolished by the removal of the occipital lobes, but it could be relearned. Careful control observations showed that the discrimination was based on a recognition of the difference in intensity of the two lights and not on any other cues.

A further analysis of this residual visual ability has demonstrated that although the perception of objects, i. e., form, position, distance, etc., was abolished in the animals which had undergone an occipital lobectomy, the capacity to discriminate intensity of light was only slightly impaired. This capacity was measured quantitatively by determining the smallest difference between the two lights which the dog could successfully distinguish. In the particular situation employed in these experiments, normal dogs could discriminate accurately between two lights the intensities of which were in the ratio of 1.2 : 1; after bilateral occipital lobectomy they failed to distinguish differences smaller than 2 : 1 or 2.5 : 1.

Experimental study of conditioned reflexes has furnished additional data on the nature of the residual sensitivity to light. Conditioned responses of blinking at the sudden exposure of a light were established by presenting the light repeatedly with a puff of air directed against the cornea. After fifty or sixty presentations of the stimuli the light alone elicits the blinking. With further reenforcement the response gains in amplitude, speed and stability.[7] This conditioned reflex to light was readily acquired by animals in which the occipital lobes were

7. Hilgard, E. R., and Marquis, D. G.: Acquisition, Extinction, and Retention of Conditioned Lid Responses to Light in Dogs, J. Comp. Psychol., to be published.

destroyed. By sensitive photographic recording of the responses it is possible to show that the conditioned reflex does not differ in any way from that of normal dogs. Moreover, the removal of the striate cortex does not destroy a conditioned reflex which was established prior to the operation. For this simple response to light the visual cortex seems nonessential. Its functions are those of fine discrimination and of spatial perception, as shown by the impairment of the threshold of sensitivity to light and the complete loss of vision for objects.

Monkeys.—Previous observations of monkeys after bilateral removal of the occipital lobes had led to the conclusion, now generally accepted, that the blindness is absolute and permanent.[5] The discovery of the residual sensitivity to light in the dog, however, made it advisable to carry out similar experiments on some animal intermediate between the dog and man.

In the monkey the area striata extends over the dorsolateral surface of the occipital lobe and along the lips of the calcarine sulcus on the cerebellar surface. By performing a radical occipital lobectomy along the line of the simian sulcus and extending forward ventrally to include the anterior limit of the calcarine sulcus it was possible to remove the area striata completely. A monkey that had undergone a unilateral operation of this type showed homonymous hemianopia of the contralateral fields, with the dividing line passing through the center of fixation. It was impossible to determine whether or not there was macular sparing. A monkey subjected to bilateral removal of the occipital lobe [8] appeared totally blind, like the dog. When moving about in unfamiliar surroundings the animal bumped into walls and objects repeatedly, until after weeks it learned to feel its way with its hands. It paid no attention to food placed before it, unless its hands or mouth in random searching happened to touch it. It did not blink or make any response to threatening movements.

When training to develop a conditioned reflex, similar to that described for the dogs, was carried out, it was found that monkeys, too, retained a slight sensitivity to light. The conditioned response could be established as rapidly in animals subjected to bilateral lobectomy as in normal monkeys. The form, amplitude and latency of the response were normal, and the course of development and extinction of the response corresponded to that found for animals that had not been operated on. Until further investigation of the threshold of sensitivity to light is carried out it will be impossible to estimate the degree of impairment, but there can be no doubt that, although all spatial perception is abolished in monkeys, a primitive sensitivity to a change in illumination is preserved.

8. Marquis, D. G.: Unpublished data.

COMMENT AND SUMMARY

It is thus apparent that in the evolutionary development from the fish to man a complete reorganization of the central visual system has taken place. In the lower vertebrates the visual functions are carried out entirely by mesencephalic centers, while in man the cortex has taken over all the optic functions with the exception of the pupillary reflex to light. This reorganization has not appeared suddenly but can be traced by gradual stages in the intermediate animals. In reptiles and birds there is a small optic projection tract to the forebrain, but these animals do not possess a true striate cortex. Within the mammalian series, from the rodents to the primates and man, there is a progressive shifting of visual functions from the superior colliculus to the striate cortex. Analysis of these functions has shown that the discriminative and spatial functions are first assumed by the cortex. In dogs and in monkeys the subcortical centers are still capable of mediating a perception of light and dark, although vision of objects is impossible. The recognition and localization of objects by their form, size, position, etc., is a spatial perception depending on the appreciation of the distribution of excitation over the surface of the retina. It follows that destruction of the cortex abolishes these spatial perceptions, while a primitive sensitivity to light may be retained.

The analogy between the organization of the visual system in the dog and the monkey and the somatic sensory system in man is immediately apparent. In both instances the destruction of the cortical area produces a marked impairment in the discriminative and spatial characteristics of perception but leaves a basic awareness of stimulation. I should like to suggest that this similarity is more than an analogy. In the light of the evolutionary development of the cortex it may well be that the difference between the organization of the visual and that of the somatic system in man represents a difference in degree of encephalization. The evolutionary change characterized by the progressive shifting of functions from the subcortical to the cortical level has merely progressed farther in the visual system than in the somatic sensory system. It would be unprofitable now to attempt to go further in the application of this phylogenetic interpretation of the organization of the cerebral afferent systems, but it is hoped that its formulation may serve as a guide to further research.

333 Cedar Street.

ABSTRACT OF DISCUSSION

DR. FRANKLIN JELSMA, Louisville, Ky.: Flourens, over a century ago, was probably the first observer who directly associated the brain with vision. Since then many careful, well planned studies have been made, so that part by part the details of the retinal projection on the cortex have been determined, until now Dr. Poljak's work suggests a plan approaching a point-to-point representation.

The results of other workers who approached the question by the anatomic and experimental methods are well in accord with a high degree of localization. Studies in the field of comparative anatomy reveal the gradual shifting of the primary visual mechanism from the optic tectum, the superior colliculus, to the geniculostriate system.

As the phylogenetic series is ascended, the higher is the degree of localization, until in man, as Dr. Marquis found, encephalization of vision has proceeded to such a point that the pupillary reflex is the only known optic response reserved for the subcortical centers.

There is considerable difference of opinion as to the amount of visual function remaining after ablation of the striate area in monkeys, dogs and cats. The difference in development and arrangement between the central optic system of the experimental animal and that of man places certain limitations on this comparison.

It is difficult to explain the degree of vision retained in certain anatomicoclinical cases in which the striate area has been badly damaged or completely destroyed. The problem is particularly difficult when the lesion has occurred in early embryonic life.

I wish to mention briefly a case that has been reported in detail elsewhere, which illustrates how gross defects of the occipital lobe and the degree of retained vision do not always coincide with the known concepts of visual localization. In such clinical instances much of the desired information for confirmation of the extent of the lesion is lacking. In one case, an effort has been made to supplant this lack of information by multiple examinations at operation.

A white boy, aged 11 years, suffered frequent seizures characterized by temporary sensations of numbness on the right side, followed by a loss of volitional motor power and increased tonicity of the extremities. The neurologic examination gave normal results in all respects. The results of the general physical examination and laboratory studies were normal. Encephalograms revealed a porencephalic cyst of the posterior portion of the left hemisphere.

At operation there was found a large cerebral defect filled with cerebrospinal fluid, communicating with the ventricle and contained within the arachnoid. The anterior margin of the defect was bounded by brain tissue, very sharply delimited, with the gray and the white substance plainly defined. The body of the lateral ventricle, with the choroid plexus protruding, was readily seen. The opening of the inferior cornu of the ventricle lay below and laterally. The lesion corresponded closely to a coronal section through the superior parietal lobule passing laterally just anterior to the angular gyrus. The falx formed the mesial confines, and the tentorium, the postero-inferior boundaries. There was no evidence of degenerated, atrophied or compressed cerebral tissue remaining. The dura was adherent to the superior margin of the brain tissue.

Occasion arose to reelevate the flap. Again air was introduced beforehand and roentgenograms were made. More observers, including Dr. Marquis, were on hand. Photographs and drawings were made. Similar defects were dissected out in the brains of cadavers, and the extent of the defects was estimated.

We are certain as to the absence of the occipital lobe and more and are unable to account for the normal macular, monocular and binocular vision, with only slightly constricted right homonymous defects of the fields, and normal zonal sensitivity to color.

Surely some part of the cortex has assumed the function of the absent visual centers.

Dr. Alfred T. Steegmann, Cleveland: The anatomic structure of the central visual system in primates is similar to that of man. Dr. Poljak has not only

verified the results of previous experimenters such as Brouwer but has added to anatomic knowledge much that is new and that will be of great clinical value.

Dr. Marquis has applied the methods used in physiologic and experimental psychologic research to problems which have ordinarily been considered purely anatomic. In addition, he has emphasized the importance of encephalization in explaining the differences between the visual function of man and that of the lower animals.

Investigation of the central visual system in pathologic conditions in man is beset with many difficulties. Perhaps the commonest and most favorable lesions for study in the striate cortex are those due to vascular occlusion with the resulting ischemic softening of the brain. Such lesions, however, are frequently multiple and may involve the visual fibers in both hemispheres. The areas of softening follow the blood supply rather than a more desirable localized area in a certain part of the striate cortex.

In working with human material one often discovers cases in which a suitable cerebral lesion is seen but in which clinical information, particularly the determination of the visual fields, is lacking.

These points illustrate why experimental studies such as those reported today are of great importance.

Dr. E. E. Blaauw, Buffalo, N. Y.: Ophthalmologists as well as neurologists are much interested in the great physiologic problems of vision.

In searching for an explanation of sight one must, first of all, consider the region of the calcarine fissure. The finer details were first investigated in the laboratory at Amsterdam.

Drs. Poppelreuter, Goldstein and Gelb and others have analyzed the physiologic changes in cases of severe traumatism of the occipital lobe.

I wish Dr. Poljak would say something about his observations on the retina because the texture of the retina is of particular interest to ophthalmologists.

Dr. Stephen Poljak, Chicago: There are two observations concerning the central part of the visual system that I have contributed. One is the arrangement of the various quadrants in the visual radiation, which was previously not known: Any one who wants to convince himself of this can read the monograph of R. A. Pfeifer, which was published in 1925. It deals with the entire history of the question of visual radiation and presents the author's view on the basis of his own research. Pfeifer was a pupil of the famous Flechsig and probably used Flechsig's material also. His presentation of the visual radiation is completely confused. Perhaps I should not use such a harsh expression, but I am forced to do that in reply.

Up to the present time it was not known where the upper peripheral quadrant, the lower peripheral quadrant and the macula were represented in visual radiation. Different scientists searched for the "macular bundle" in the uppermost or in the lowermost part of the visual radiation, or wherever they pleased. I think that the experiments I have presented clearly show that this structure is neither in the upper nor in the lower part but exactly in the center.

The other thing is that Brouwer and his pupils in their latest articles have frankly admitted that although they gave evidence of a quadrantic projection of the retina, it is not known whether there is anything beyond this resembling what is known as the point-to-point representation of the retina in the cerebral cortex. Such a detailed projection, of course, was assumed by others, and, I admit, that assumption was made long ago. Eighty years ago Helmholtz postulated the existence of such a projection. Students of the physiology of vision have always believed that in the center of vision, which corresponds to the central part of the fovea, a single impulse hitting a single cone must, as a single impulse, reach the

cortex; but whether this was true was not known. There was no anatomic proof. What my colleagues and I are trying to do now is to help students of physiology, who are really far ahead of us, to explain by means of the anatomic approach that which they have always believed.

I should like to touch on the question of the retina. One does not know what takes place in the retina, for one does not know enough about its organization. The last word about the fine organization of the retina was given forty years ago by Ramón y Cajal.

The first preparation of sections of the monkey's retina that I made by Golgi's method showed that structure to be far more complex than was formerly believed. Many types of cells are present; some have a very fine discriminatory function by means of which the principle of a point-to-point contact between the neurons is realized. Besides these fine mechanisms there are others which are more diffuse.

Among the the bipolar cells are those which I called midget bipolar cells, each connecting a single cone with a single midget ganglion cell. There are other bipolar cells which connect twenty-five and perhaps as many as a hundred or more of the cones and rods with one or a few of the ganglion cells. There is even a variety of ganglion cell which is in contact with thousands of the various bipolar cells.

The retina is such a complicated organ that its study throws a new light on the entire visual system. Of course, many other things which have heretofore been accepted will have to be examined and tested on the basis of the new observations.

Dr. Donald Marquis, New Haven, Conn.: The interesting case of occipital porencephaly with essentially normal vision described by Dr. Jelsma is indeed puzzling. Through the courtesy of Dr. Jelsma and Dr. Spurling I was able to see this patient last November and to witness the operation at that time. My observations agreed essentially with the published report of the case. From notes and sketches made at the time of the operation, I was able later to dissect a brain to show the extent of the porencephalic defect. The volume of tissue removed in the dissection was equal to the volume of the defect determined roughly at operation by filling the cavity with saline solution. The entire occipital lobe, with the complete calcarine fissure, was lacking.

Since it is apparent that the removal or destruction of such a portion of tissue in an adult would produce hemianopia, I think that one is forced to conclude that the porencephaly was a prenatal developmental defect, probably beginning before the geniculocortical radiation was laid down. The visual radiation is one of the last projection systems of the cortex to be formed, according to the recent investigations of Dr. Tilney.

Two possible anatomic interpretations of the retention of normal visual fields in the absence of the occipital lobe may be mentioned. In the light of the phylogenetic evidence reported in my article, it is conceivable that the projection of the retina on the superior colliculus became more adequate in the absence of any functioning of the occipital cortex, so that there was normal spatial perception. This seems unlikely, however, since there was no essential difference between the left and the right field, one of which commanded a normal visual cortex. It is more probable, I think, that the fibers of the geniculocortical radiation, which was not formed until after the porencephalic defect had appeared, grew to another region of the cerebrum, probably in the adjoining parietal lobe, and there established under the influence of the growing fibers a visual projection area. The final answer to these extremely interesting questions can, of course, be obtained only by making a histologic study of the brain.

VISUAL PATHWAYS IN MAN WITH PARTICULAR REFERENCE TO MACULAR REPRESENTATION

WILDER PENFIELD, M.D.

JOSEPH P. EVANS, M.D.

AND

J. A. MacMILLAN, M.D.

MONTREAL, CANADA

As the result of many contributions to the study of the visual system the main features of its pathway within the brain have been well established. But the question of bilateral cortical representation of macular vision has not been satisfactorily settled, and it is with this problem and with the course of the geniculocalcarine radiation in man that this communication deals.

Study of the defects of the visual fields in patients who have undergone radical extirpation of carefully charted areas of the occipital and temporal lobes has led us to certain definite anatomic [1] conclusions. The extirpations were done for the removal of cerebral cicatrices in cases of focal epilepsy. Because of this circumstance there was opportunity for considerable study and comparison before and after operation. In many of the published reports anatomic conclusions have been drawn from observations on cases of brain tumor, in which the normal structure may be greatly displaced by the expanding lesion, or on cases of gross cerebral injury without careful surgical inspection and without autopsy to establish the exact extent of the destruction. To avoid this difficulty we have included no observations on cases of cerebral neoplasm. The craniotomies have been wide, and the location of the scar and surrounding cerebral tissue to be removed have been identified when possible by electrical stimulation, by measurements and by drawings executed during the operation. The excised tissue has further been studied grossly and, in the last case reported, microscopically from the point of view of cerebral localization.

Read at the Sixtieth Annual Meeting of the American Neurological Association, Atlantic City, N. J., June 1934.

From the Department of Neurology and Neurosurgery and the Department of Ophthalmology, McGill University and Royal Victoria Hospital.

1. The words "anatomic, "physiologic" and "hypothetic" are used in order to conform with the terminology adopted by the Archives of Neurology and Psychiatry. The authors would prefer to use the terms "anatomical," "physiological" and "hypothetical."

REVIEW OF THE LITERATURE

It is unnecessary here to review the general aspects of the excellent work on visual pathways done by Henschen,[1a] Elliot Smith, Marie and Chatelin,[2] Holmes,[3] Brouwer,[4] Putnam,[5] Poliak[6] and many others.[7] Much of the extensive clinical literature of the last sixty years is of little use for the present purpose because no study was made of loss or retention of central vision. A large number of clinical reports must be discarded because of the failure to make careful and timely perimetric examinations and because of the vagueness of localization.

In 1909 Lenz,[8] on the basis of clinical observations, suggested the possibility of a crossing tract of fibers from the geniculate body of one side through the posterior portion of the corpus callosum to the occipital

1a. Henschen, S. E.: Sur les localisations dans le ganglion géniculé extrene, Rev. neurol. **5**:619, 1897.

2. Marie, P., and Chatelin, C.: (*a*) Les troubles visuels dus aux lésions des voies optiques intracérébrales et de la sphère visuelle corticale dans les blessures du crâne par coup de feu, Rev. neurol. **28**:882, 1915. (*b*) Les troubles visuels consécutifs aux blessures des voies optiques centrales et de la sphère visuelle corticale: Hémianopsies en quadrant supérieur; hémiachromatopsies, ibid. **29**:138, 1916. (*c*) Scotomes paramaculaires hémianopsiques par lésion occipitale et scotome maculaire par lésion rétinienne unilatérale chez le même blessé, ibid. **30**:112, 1916.

3. Holmes, G.: A Contribution to the Cortical Representation of Vision, Brain **54**:470, 1931; The Cortical Localization of Vision, Brit. M. J. **2**:193, 1919.

4. Brouwer, B.: Ueber die Projektion der Makula auf die Area striata des Menschen, J. f. Psychol. u. Neurol. **40**:147, 1930.

5. Putnam, T. J.: Studies on the Central Visual Connections: III. The General Relationships Between the External Geniculate Body, Optic Radiation and Visual Cortex in Man; Report of Two Cases, Arch. Neurol. & Psychiat. **16**:566 (Nov.) 1926; Studies in the Central Visual System: IV. The Details of the Organization of the Geniculostriate System in Man, ibid. **16**:683 (Dec.) 1926.

6. Poliak, S.: The Main Afferent Fiber Systems of the Cerebral Cortex in Primates, University of California Publications in Anatomy, Berkeley, Calif., University of California Press, 1932, vol. 2.

7. Cushing, H.: Distortions of the Visual Fields in Cases of Brain Tumor, Brain **44**:341, 1922. Von Economo, Constantin: The Cytoarchitectonics of the Human Cerebral Cortex, translated by S. Parker, New York, Oxford University Press, 1929. Frazier, C. H., and Waggoner, R. W.: Tumors of the Occipital Lobe: A Review of Forty Cases, Arch. Neurol. & Psychiat. **22**:1096 (Nov.) 1929. Meyer, A.: The Connections of the Occipital Lobes and the Present Status of the Cerebral Visual Affections, Tr. A. Am. Physicians **22**:7, 1907. Roenne, H.: Ueber doppelseitige Hemianopie mit erhaltener Makula, Klin. Monatsbl. f. Augenh. **53**:470, 1914. Traquair, H. M.: Fields of Vision in Intracranial Lesions, Brit. M. J. **2**:229, 1933.

8. Lenz, G.: Zur Pathologie der cerebralen Sehbahn under besonderer Berücksichtigung ihrer Ergebnisse für die Anatomie und Physiologie, Arch. f. Ophth. **72**:1 and 187, 1909.

lobe of the other side. The exact course of these fibers which he assumed to subserve macular vision is not clear.

Marie and Chatelin [2a] in 1915 made an exhaustive study of gunshot wounds of the occipital lobe. The visual fields which they presented show that in many cases there was sparing of central vision on the blind side, but the authors did not offer an explanation of the sparing of the maculae.

Holmes and Lister [9] in 1916 reviewed a somewhat similar series of cases of gunshot wounds. They produced evidence that macular vision is represented exclusively in the tip of the occipital lobe and reported a case of complete loss of central vision with sparing of peripheral vision due to a gunshot wound which had injured the tip of each occipital lobe. The extent of this injury was determined by surgical inspection. This point of view was in agreement with that of Marie and Chatelin.

Wilbrand and Saenger [10] in 1917, on reviewing their clinical material, concluded that there must somehow be bilateral cortical representation of macular vision, and Pfeifer [11] in 1925 suggested that there is in man a tract which becomes separated from the ventral portion of the geniculocalcarine radiation (inferior longitudinal fasciculus) and that this tract of fibers crosses by way of the corpus callosum to the opposite hemisphere. This tract Foerster [12] (1929) regarded as carrrying fibers which have to do with macular vision; he added the report of a case which tended to confirm this point of view and which will be described later.

Allen [13] in 1930 reviewed the reports of forty cases of tumor of the occipital lobe and found that in certain cases homonymous hemianopia with sparing of macular vision was noted, while in other cases the macula was found definitely to be split. Horrax and Putnam [14] (1932), reporting a like number of cases of tumor of the occipital lobe, found that a large proportion of their patients (73.6 per cent) with tumor confined to or chiefly compressing the occipital lobe had contralateral homonymous hemianopia with sparing of central vision. This, they stated, was particularly true in the patients with meningioma situated at

9. Holmes, G., and Lister, W.: Disturbances of Vision from Cerebral Lesions with Special Reference to the Cortical Representation of the Macula, Brain **39**:34, 1916.

10. Wilbrand, H., and Saenger, A.: Handbuch der Neurologie des Auges, Wiesbaden, J. F. Bergmann, 1917, vol. 7.

11. Pfeifer, quoted by Foerster.[12]

12. Foerster, O.: Beiträge zur Pathophysiologie der Sehbahn und der Sehsphäre, J. f. Psychol. u. Neurol. **39**:463, 1929.

13. Allen, I. M.: A Clinical Study of Tumors Involving the Occipital Lobe, Brain **53**:194, 1930.

14. Horrax, G., and Putnam, T.: The Field Defects and Hallucinations Produced by Tumors of the Occipital Lobe, Brain **55**:499, 1932.

the posterior end of the occipital lobe. They suggested that the sparing of fibers was characteristic of lesions of the occipital lobe, whereas bisection of the macula was most frequent in cases of tumor of the temporal lobe.

Foerster and one of us (W. P.) [15] in 1930 reported one case of gunshot wound of the occipital lobe with extensive damage of this lobe, confirmed at operation. There was associated homonymous hemianopia, with sparing of the central field. In a second case of gunshot wound of the occipital lobe a paracentral scotoma was found preoperatively, the significance of which will be considered later. Excision of the occipital pole resulted in a conversion of this defect of the field into homonymous hemianopia with sparing of macular vision.

EXCISION OF THE TEMPORAL LOBE

CASE 1.—*Posttraumatic epilepsy with cerebral cicatrix; amputation of the right temporal lobe.*

R. M., a young man, referred by Dr. W. F. Hamilton, Montreal, had received a severe injury to the head at the age of 8, associated with hemiplegia which gradually disappeared. Subsequent to the injury there developed jacksonian seizures which began in the left hand.

The first surgical procedure was carried out when the patient was 20. A small cicatrix on the precentral gyrus in the hand area was removed (fig. 1). A portion of cicatrix was also removed from the temporal lobe, but the patient's unfavorable condition prevented further surgical intervention.

A second operation was carried out two years later. The right temporal lobe was very thin over the inferior horn of the lateral ventricle. The lobe was partially gelatinoid but reacted to stimulation. It was excised completely (fig. 1). This left the ventricle open and the island of Reil exposed.

Examination of the visual fields has been carried out repeatedly by one of us (J. A. MacM.). The patient has complete homonymous hemianopia which splits macular vision in the center (fig. 2).

Although the following observation is aside from the main thesis of this communication, it is interesting to note that the patient is often reminded of his visual defect by running "head on" into pedestrians on the sidewalk and even into vehicles on the street. This difficulty in his case is much more marked than is usual. A careful study has suggested to us an explanation of this difficulty. His blind field is to his left, but he habitually carries his head turned to the right and his eyes, whenever they shift from fixation, deviate still further to the right (fig. 3) and back again. He can and does, by conscious effort, correct the deviation, but when his attention is distracted the head deviates, and although the eyes focus on the object of his attention they periodically swing out to the right and then back to the fixation point, never deviating to the left. This causes him to expose the blind portion of the retina to whatever lies before him.

Why should he continue to do this when the natural compensatory and corrective movement would seem to be deviation of the head and eyes to the blind side so that his seeing field would lie in front of him? Our explanation is that

15. Foerster, O., and Penfield, W.: Der Narbenzug am und im Gehirn bei traumatischer Epilepsie, Ztschr. f. d. ges. Neurol. u. Psychiat. **32**:125, 1930.

the complete removal of the right temporal lobe back to and including the head-and-eye-turning area (field *22*) has upset the normal deviation balance. A stimulatory influence on this area would cause the eyes to deviate to the left, and so,

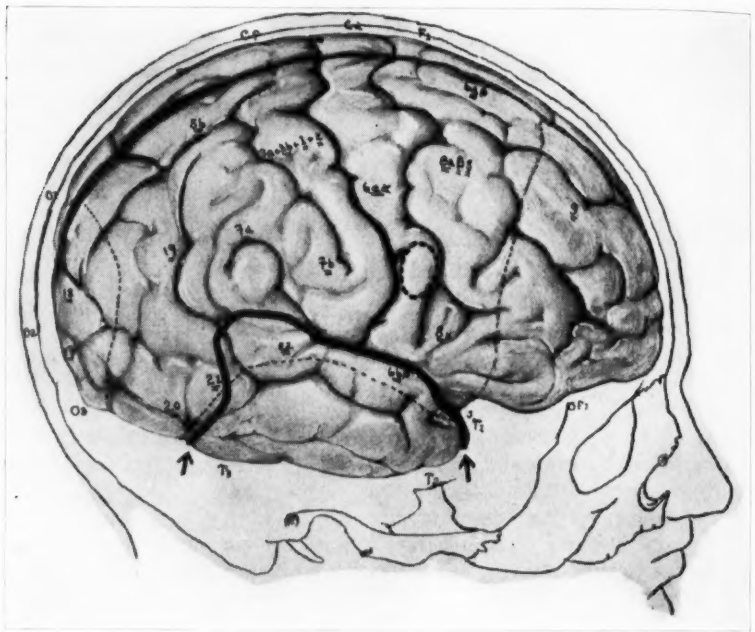


Fig. 1 (case 1).—A diagram showing the extent of resection, with the dotted line outlining the tissue excised at the first operation, the solid line and arrows indicating the extent of excision at the second operation three and one-half years later.

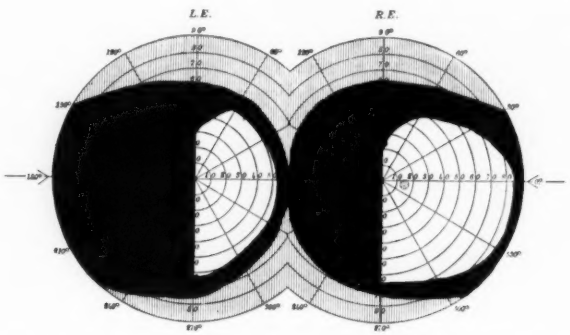


Fig. *2* (case 1).—Visual fields taken thirteen months postoperatively, showing loss of macular vision following the second operation.

contrariwise, its absence might cause spontaneous drifting of gaze toward the side of operation, the right. This turning of the head to the right with the occasional drifting of the eyes still farther to the right results in the unfortunate collisions.

Fig. 3 (case 1).—The head is held to the left, and the eyes deflect periodically from the object observed still farther to the right. There are no spontaneous swings from the point of fixation to the left.

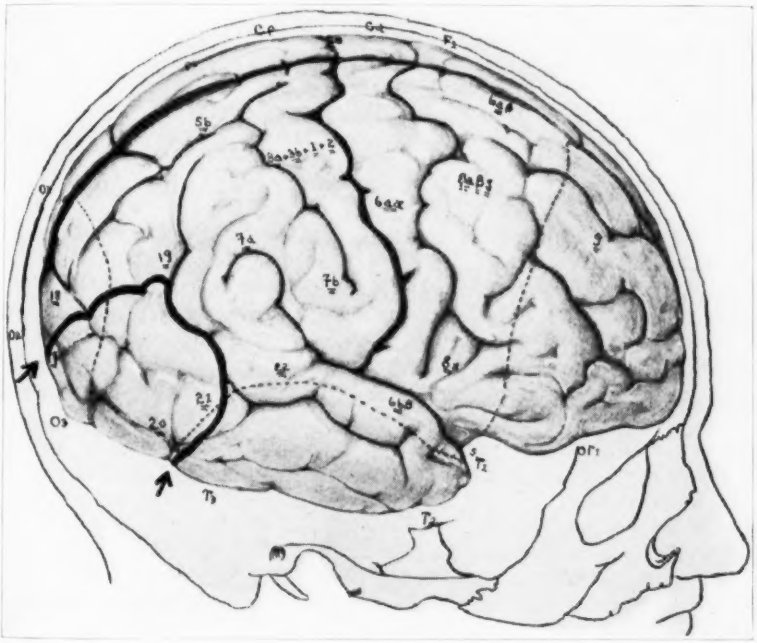


Fig. 4 (case 2).—A diagram showing the extent of excision, outlined by the heavy black line.

CASE 2.—*Focal epilepsy, cicatrix of the right posterior temporal region; radical extirpation.*

M. S., a woman, aged 21, was referred by Dr. Herbert Ross, Montreal, with a history of injury sustained at birth and convulsions starting at the age of 11 years. The results of investigation pointed to a lesion in the posterior parietal region, and encephalography showed circumscribed cerebral atrophy in the right posterior parieto-occipital region.

At operation the pathologic area was removed with a surrounding zone of from 0.5 to 1 cm. of normal cerebral tissue (fig. 4). By the excision the ventricle was opened widely at the junction of the posterior end of the ventricular body with the inferior horn. The removed area slanted off from this defect.

Detailed perimetric examination thirty-eight days postoperatively revealed complete left homonymous hemianopia including central half-vision. This observation was confirmed fourteen months after operation (fig. 5).

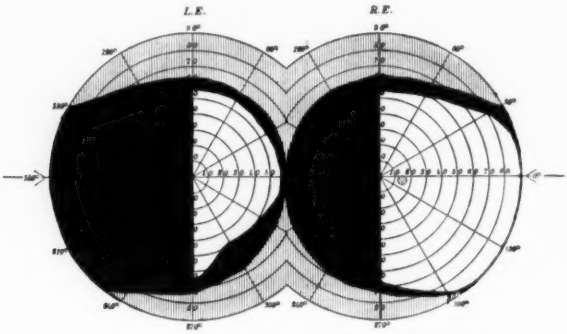


Fig. 5 (case 2).—Visual fields charted fourteen months postoperatively.

AMPUTATION OF THE OCCIPITAL LOBE

CASE 3.—*Focal epilepsy secondary to cerebral embolism; left occipital lobectomy.*

L. K., a girl, aged 15, was referred by Dr. Walter Phillips, of Englewood, N. J. She had suffered multiple fractures at the age of 8 in an automobile accident. During convalescence she suddenly became blind on two occasions and had several attacks of jacksonian seizures on the right side. Evidently at that time she had a cerebral embolism. At the end of 6 months she began to have epileptiform manifestations of stars in the right visual field, which appeared daily. These came to be associated with convulsions on the right side. Examination of the visual fields at times revealed a partial homonymous defect on the right side. This defect seemed to increase a little during the two years in which we studied her condition. Encephalography showed marked selective atrophy of the left occipital and temporal lobes and a cyst in the occipital lobe.

Occipital osteoplastic craniotomy on the left side was carried out on March 4, 1927, and the occipital lobe was amputated (fig. 6). The line of excision crossed the ventricle, and the removed block measured 7 cm. anteroposteriorly, 6 cm. from above down and 3.7 cm. from side to side.

Postoperatively there was right homonymous hemianopia, but examination by Dr. William Cone at that time revealed preservation of macular vision (fig. 7). Two months after the operation the patient was examined in detail by Dr. Mark Schoenberg, who found preservation of central vision. His report was:

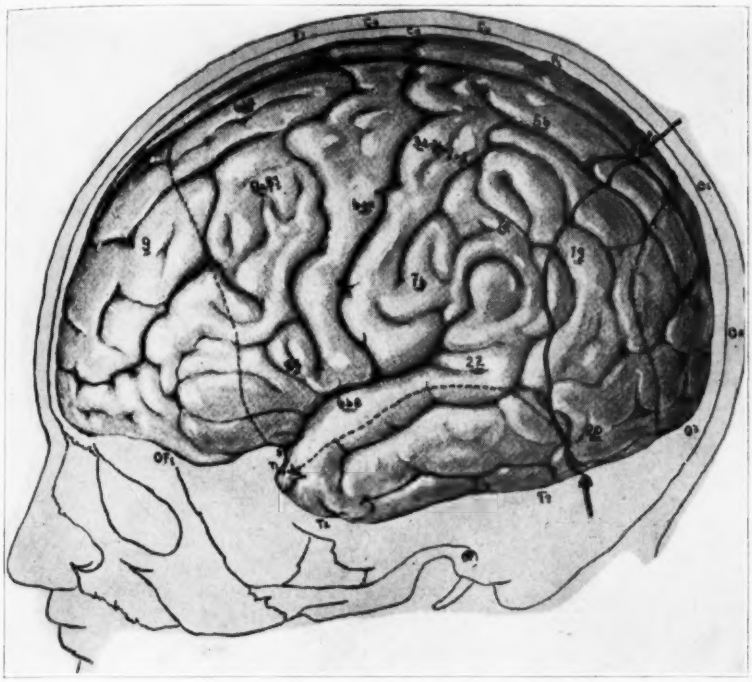


Fig. 6 (case 3).—A diagram showing the extent of excision, outlined by the heavy black line and indicated by arrows.

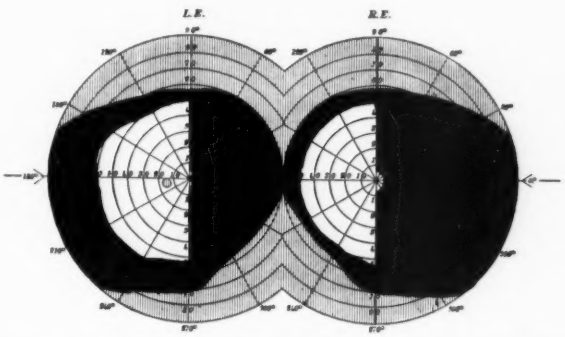


Fig. 7 (case 3).—Visual fields charted three weeks postoperatively, showing preservation of macular vision. A 2 mm. white test object was used.

The patient came to me on May 7, 1927, and I found right homonymous hemianopia. Vision in the right eye was 20/20 plus and in the left eye 20/20 minus. With the right eye she read very small type (Birkhauser 1); with the left eye she read 0.9 type. In other words, vision in the left eye was not as completely normal as that in the right eye. When the sense of color was tested on the Stilling tables a slight disturbance of color vision was noted; namely, she could not read the 4's in group 1, table 1; she had difficulty with groups 5 and 9 in table 1. Her reading was slow. She could thread a needle well with both eyes open, but not with one. She complained that at times she saw in the right side of the field near her right cheek "two stars like water of no particular color, standing still in space." This would last from a few seconds to about half an hour and would appear twice or several times daily.

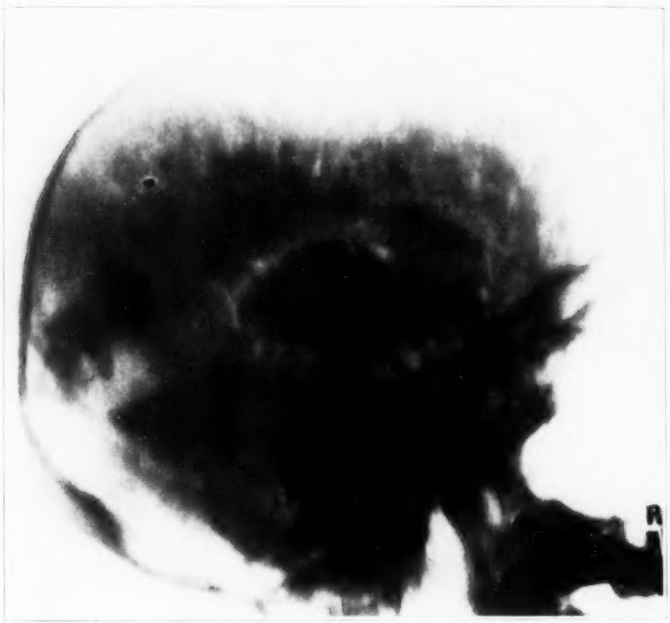


Fig. 8 (case 4).—Encephalogram showing the location of the calcified sterile abscess.

In the years since surgical intervention this aura has persisted, which is evidence that visual sensations may be produced in the absence of the calcarine cortex.

CASE 4.—*Focal epilepsy due to calcified abscess of the occipital lobe; left occipital lobectomy.*

L. P., aged 14, who was referred by the late Dr. Michael Osnato, New York, had suffered for four and one-half years from epileptic seizures which began with an aura of colored stars on the right. He wrote with his right hand but did everything else with his left hand by preference. He had a defect in the lower quadrant in the right homonymous field, and encephalograms showed calcification above and mesial to the enlarged posterior ventricular horn (fig. 8).

Left occipital osteoplastic craniotomy was carried out, and the occipital pole was excised with the calcified sterile abscess which was in it (fig. 9).

Fig. 9 (case 4).—A diagram showing the extent of resection of the occipital pole, outlined by the heavy black line and indicated by arrows.

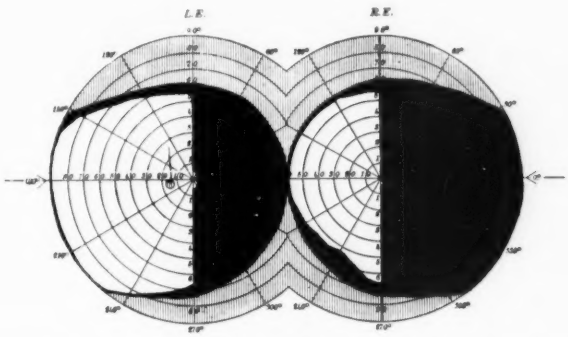


Fig. 10 (case 4).—Visual fields charted one month postoperatively.

The ophthalmologic report (by J. A. MacM.) one month after operation was: Vision in the left eye was 6/6 and in the right eye, 6/36. The fields showed right homonymous hemianopia (fig. 10). The maculae were spared in both eyes.

CASE 5.—*Focal epilepsy due to cicatrix of the right occipital lobe; amputation of the right occipital lobe.*

C. F., a youth, aged 18, who was referred by Dr. H. E. Ridewood, Victoria, B. C., gave a past history that was essentially irrelevant except for a fall from a bicycle at the age of 11. He expressed the opinion that he struck the back of his head. He was rendered dazed but not unconscious and remained in bed one day.

At the age of 14 he had the first epileptic seizure; since then six or eight more had occurred. The attacks were characterized by a "pulling sensation in the eyes," associated with a feeling as of a shade being drawn across the left half of the field of vision. Blurring of vision followed, and subsequently numbness and stiffness of the left hand were noticed and then forced turning of the head

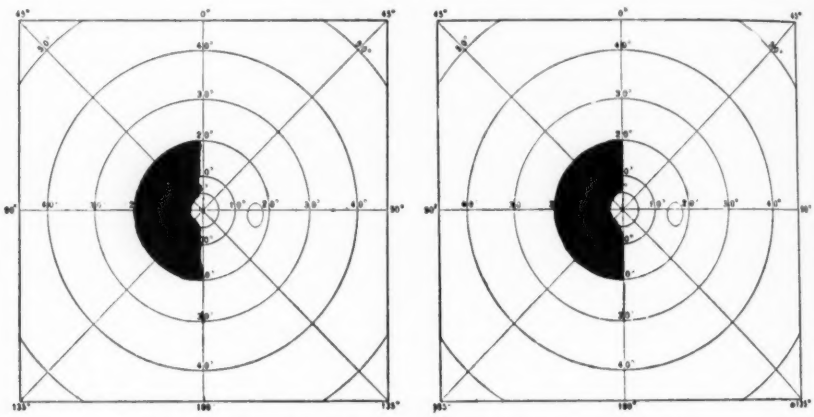


Fig. 11 (case 5).—Visual fields charted postoperatively.

to the left; loss of consciousness and a generalized convulsion followed. There were frequent lesser attacks which resembled the first stages described, without generalized convulsions.

Examination of the visual fields before surgical intervention revealed left homonymous hemianopia on vis-a-vis perimetry and definite sparing of macular vision on detailed perimetric examination (fig. 11). After each succeeding attack the patient had observed increasing darkness in the left homonymous field and the observation was borne out by perimetric studies made by Dr. Scott-Moncrieff of Victoria six months before operation (fig. 12).

Encephalograms showed evidence of an atrophic lesion limited to the right occipital pole (fig. 13). An occipital osteoplastic craniotomy on the right side was done, and when the dura was reflected dense adhesions were found. The descriptive note dictated by one of us (W. P.) immediately after the operation read: These adhesions became more dense at the tip of the occipital pole, where they were replaced by a very dense scar which passed inward beneath the occipital lobe. The ventricle extended backward into a cyst on the surface of the brain at the junction between the falx and the tentorium. This was the site of the more

intense adhesions. Therefore, the wall of the ventricle was replaced by a membrane here. When the fluid was allowed to escape from the cyst there appeared an excavation, so that it seemed that the whole calcarine area had been destroyed. The area of destruction passed forward and downward to the hippocampal gyrus, where it seemed to stop abruptly. The convolutions of the occipital lobe on its lateral aspect seemed a little small and were somewhat flattened.

The occipital pole was removed in a block by silk sutures. The measured distance of the line of removal from the torcula forward along the longitudinal sinus was 5 cm. The measured distance from the torcula laterad along the horizontal sinus was 5.5 cm. (Measured distances from fixed points within the skull are somewhat misleading in this case because the atrophy of the occipital lobe together with the pull of the contracting cicatrix had served to displace the remaining structure of that part of the hemisphere backward. This error would mean that the portion removed included more, not less, of the hemisphere than was estimated.)

The area removed passed perpendicularly downward to the posterior end of the corpus callosum. It followed the hippocampal gyrus below and exposed the

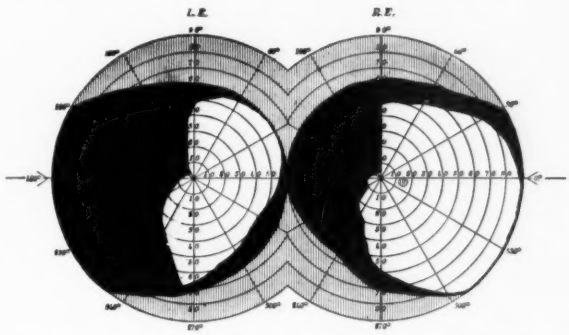


Fig. 12 (case 5).—Visual fields charted six months before the patient's admission to the hospital, showing partial preservation of left homonymous fields at that time.

edge of the tentorium from the midline outward until it disappeared passing forward. No mesial surface of the occipital pole was left behind if the pole is considered as that part of the brain which is behind the vein of Galen. It is doubtful that any of the calcarine fissure was left.[16] The original excision cut across the ventricle and left a large part of the choroid plexus projecting.

Amputation of the lobe in this case was similar in extent to that in case 3, with the exception that in this case removal extended farther forward at the midline. The corpus callosum was reached, whereas in case 3 some tissue was left adjacent to that structure. The extent of removal of the lobe as indicated by encephalography is shown in figure 13, and figure 14 is the artist's drawing of the site of excision.

The specimen was examined carefully. There was no tissue which could be suspected of being visual cortex in the posterior end of the occipital lobe. Farther

16. By that was meant that the whole of the calcarine area was believed to have been destroyed by the atrophic process and replaced by the cyst before surgical intervention.

forward on the mesial aspect of the lobe was a zone about 5 mm. in diameter where histologically the arrangement of the cortical cells betrayed the fact that these cells were of the calcarine type. It was impossible to say whether or not the afferent pathway to these cells was intact.

Recovery was uneventful, and repeated examination of the fields revealed that a change had occurred. The macula-sparing homonymous hemianopia had been

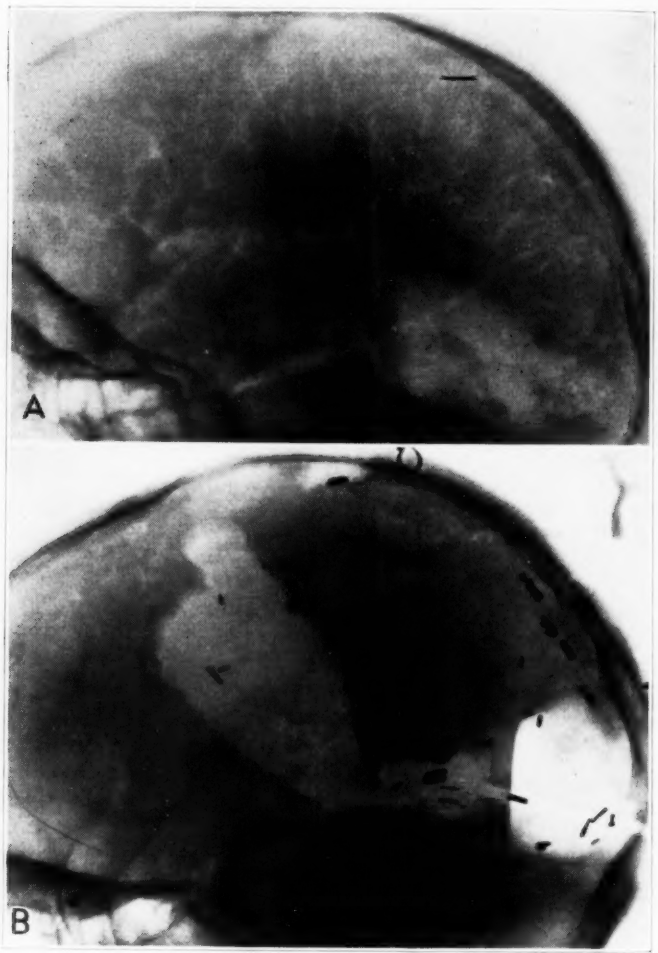


Fig. 13 (case 5).—*A*, an encephalogram made preoperatively with air in the posterior horn, shows the extent of atrophy of the occipital lobe. *B*, made postoperatively, shows the magnitude of removal of the occipital lobe which was outlined by silver clips. Air is seen in place of the occipital pole.

converted into a macula-splitting homonymous hemianopia (fig. 15). This could be definitely determined despite a tendency to the development of nystagmus on maintaining fixation.

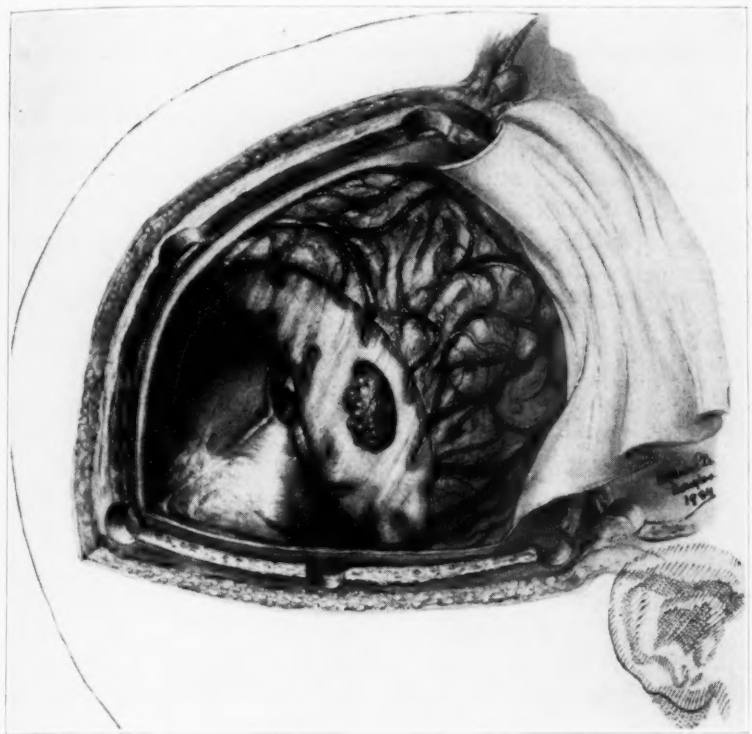


Fig. 14 (case 5).—An artist's drawing of the extent of removal, elaborated from the surgeon's sketch made at operation.

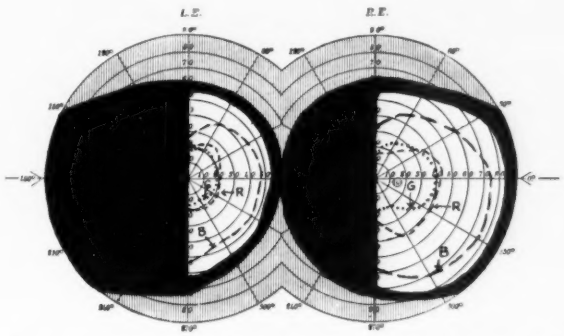


Fig. 15 (case 5).—Visual fields charted five weeks postoperatively, showing bisection of the maculae.

COMMENT

Review of the literature has failed to reveal a single case that will satisfy the requirements of a physiologic experiment and settle beyond doubt the factors that determine loss or sparing of the maculae. The possible exception is the case cited by Foerster,[12] that of a patient in whom a tumor was suspected in the region of the corpora quadrigemina. To approach the area in question the corpus callosum was incised to a depth of 2 cm., and the posterior end of the right occipital lobe was amputated about 5 cm. from the tip. The visual fields before operation were normal; postoperatively they showed complete left homonymous hemianopia passing through the fixation point.

Because of the fact that removal of the occipital lobe in other cases had resulted in hemianopia with sparing of macular vision, Foerster attributed the split macula in this case to the incision of the splenium. He concluded, therefore, that fibers subserving crossed macular representation pass to the opposite hemisphere in the posterior portion of the corpus callosum. As evidence of the existence of such a tract he cited the anatomic observations of Pfeifer.

Putnam,[5] who based his conclusions on myelogenic studies of a baby's brain—work similar to that done by Pfeifer—was unable to verify Pfeifer's observations of a bundle from the geniculocalcarine radiation to the corpus callosum in man. Horrax and Putnam [14] concluded that proof of the existence of a crossing tract is lacking.

To leave the question of this tract for the moment, it seems evident that interference with the geniculocalcarine radiation (inferior longitudinal fasciculus) in the posterior portion of the temporal lobe leads to complete homonymous hemianopia involving all fibers and including those of central vision (cases 1 and 2). Further, extensive removal of the occipital lobe including what seems to be all of the area striata can be carried out with sparing of macular vision. This was proved by actual resection in cases 3 and 4 and by gross examination of the previously destroyed lobe in case 5, in which only a fragment of visual cortex remained and that far anterior.

The necessity of great care in recording visual fields cannot be overstressed. The peripheral fields in this series have been taken, when possible, on the arc perimeter, and central vision has been examined with the Bjerrum screen. In instances in which the campimeter has been used that fact is indicated by the recording of the focal distance of 110 mm. The size of object used is likewise indicated on the perimetric chart. We have found it helpful in testing central vision to have a second observer focus his attention on the subject's eye so that the slightest deviation from fixation may be indicated at once.

Preservation of central vision in man after removal of the calcarine area might be explained in one of two ways: Either there is cortical representation of the macula anterior to the occipitoparietal fissure or there is a tract which crosses to the opposite area striata.

In the first instance the accessory macular bundle would have to end in cortex the structure of which differs microscopically from that of the area striata. This would mean a radical departure from the accepted principles of the relation of cortical structure to function. A further argument against such an explanation is the demonstration by Holmes

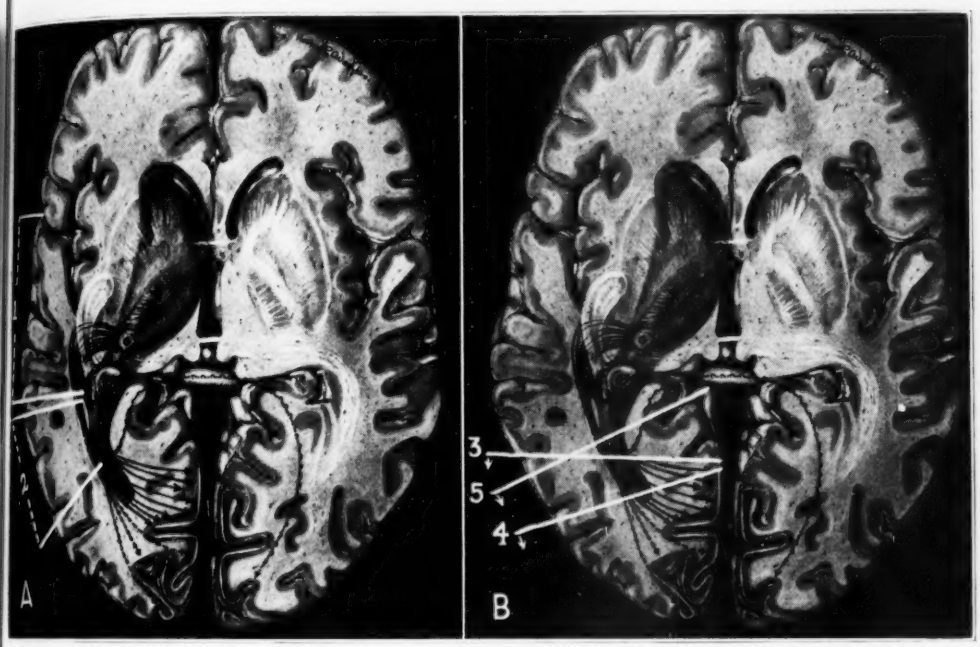


Fig. 16.—*A* is a drawing to schematize the extent of removal in cases 1 and 2, in which there was complete homonymous hemianopia. For convenience both are considered to be on the left side. *B* is a drawing to show the extent of removal of the occipital lobe in cases 3, 4 and 5. In cases 3 and 5 all the visual cortex seems to have been removed, but the hypothecated crossing tract, indicated by the lines made up of question marks, has escaped, resulting in homonymous hemianopia with sparing of the central field.

and Lister[9] that a gunshot wound which injured the tips of both occipital lobes produced a complete central scotoma, leaving peripheral vision intact. The peripheral vision evidently was represented anteriorly. It seems unlikely, to say the least, that the bullet could have destroyed both occipital poles and also two hypothetical anterior areas of macular representation, at the same time sparing the intervening area

striata, where peripheral vision is represented. This is in conformity, moreover, with the posterior cortical representation of macular vision in the monkey (Poliak [6]).

Therefore, the existence of macular representation anterior to the occipitoparietal fissure seems doubtful. The remaining explanation is the existence in man of a group of fibers subserving macular vision which crosses to the opposite hemisphere and terminates in the tip of that occipital pole. What the course of these fibers is has been open to question. Lenz indicated that they cross in the posterior portion of the corpus callosum, and Foerster suggested that they may cross in the posterior 2 cm. of the splenium.

By plotting carefully the extent of our excision we gained tangible evidence as to the course of the geniculocalcarine radiations, and there

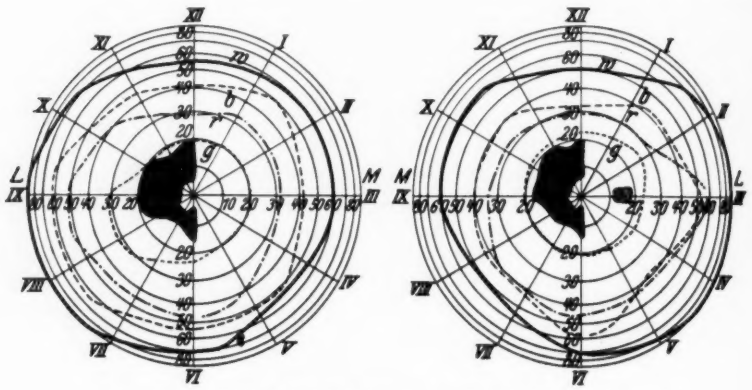


Fig. 17.—Visual fields in Foerster and Penfield's case 4.

is enough positive and negative evidence to trace out an approximate pathway for the crossing macula bundle if it exists. As indicated in figure 16, it must swing laterally and backward about the ventricle with the fibers destined for the macular representation of the same side. At about the level where the inferior longitudinal bundle meets the arching fibers of the splenium this aberrant macular bundle must turn forward and mesiad to cross the midline in the splenium and travel to the macular area of the opposite visual cortex.

On the basis of the course of the crossed tract just indicated it becomes easy to explain the observations in case 5. The homonymous hemianopia was macula-sparing, although the calcarine area had been destroyed before surgical intervention except for a very small fragment of cortex which resembled visual architectonic. The surgical extirpation probably did not remove any functioning visual cortex; it interrupted the curving macular tract anteriorly where the line of removal reached to the splenium.

Conceding the existence of this double representation, it should be possible to cut the posterior end of the corpus callosum in an approach to the third ventricle or to the roof of the midbrain without producing a detectable disturbance in the visual fields. Neurosurgeons have frequently cut this structure without interfering with vision. It should, further, be possible to remove the macular representation at the posterior end of the occipital lobe without producing central scotoma if it is possible to do so without injuring the adjacent areas representing peripheral vision. In case 4 of those reported by Foerster and one of us (W. P.) [15] a lesion involving the tip of the occipital lobe produced a small paramacular scotoma (fig. 17). It seems likely that in this case the macular fibers of that hemisphere were actually destroyed and that in addition some of the representation of the peripheral field was ablated. The defect was apparent only in the peripheral field, as this representation is certainly not bilateral and is more strictly localized.

The final demonstration of a crossed tract subserving macular vision must await Marchi studies of a suitable adult patient. Until that time the aberrant or crossed tract must be considered to be hypothetic, however strong may be the circumstantial evidence of its existence.[17] This crossed bundle might be made up entirely of collateral fibers branching from the fibers of the direct macular bundle, and it does not necessarily follow that because Putnam was unable to trace it in an infant it does not exist in an adult.

SUMMARY

Radical extirpation of cerebral cicatrices together with surrounding cerebral tissue affords evidence of resultant anatomic and physiologic defects considerably more reliable than that provided by neoplastic or traumatic destruction of cerebral tissue.

Excision of the posterior portion of the temporal lobe produces complete interruption of the geniculocalcarine radiation and results in complete homonymous hemianopia with splitting of the macular field (cases 1 and 2). Complete removal of one temporal lobe may produce, in addition to this defect of the visual field, spontaneous habitual deviation of the eyes and head to the side of the removal.

17. On purely theoretical grounds it may be suggested that with the crossing macular fibers there may well be some crossing of those fibers which represent the zone of junction of the two hemianopic fields, a zone which if drawn on the retina would be covered by a strip passing perpendicularly through the macula. If that should prove to be true it might be found that homonymous hemianopic visual fields with maculae spared would show an irregular extension of vision across the midline into the blind field both above and below the fixation point. We have found evidence of this which may be considered only suggestive, not as verification.

Removal of a large portion of the occipital lobe, including the area commonly believed to contain all of the calcarine cortex, results in homonymous hemianopia with sparing of central vision (cases 3 and 4). If the calcarine area has been destroyed as a functional unit by a previous pathologic process (as was probably true in case 5) the hemianopia spares the macular region. If the lobe is now extirpated and the line of removal is carried forward at the midline to a level immediately adjacent to the splenium, a macula-sparing hemianopia is converted into a macula-splitting hemianopia (case 5).

The conclusion follows that either a hitherto undemonstrated representation of macular vision exists near the splenium or there is a tract of fibers subserving macular vision which leaves the inferior longitudinal fasciculus after rounding the ventricle and turns sharply mesiad and anteriorly. In our opinion the second conclusion is more likely. The evidence from our cases strongly supports the hypothesis that this tract passes to the visual cortex of the opposite hemisphere by way of the splenium. It is suggested that this aberrant geniculocalcarine bundle is composed of collateral branches from the nerve fibers in the macular portion of the direct geniculocalcarine radiation, as indicated by the hypothetic tract in figure 16 *A*.

Clinical Notes

PAROSMIA IN TUMOROUS INVOLVEMENT OF OLFACTORY BULBS AND NERVES

HARRY A. PASKIND, M.D., CHICAGO

Perversions of the sense of smell in organic intracranial disease are encountered not infrequently in lesions of the uncinate gyrus or adjacent parts of the temporal lobe. Uncinate gyrus fits, first described by Jackson and by Jackson and Beevor, produce momentary sensations of odor, usually of an unpleasant odor, accompanied or followed by a brief obscuration of consciousness. In the uncinate fit the cardinal symptoms are the momentary duration of the unpleasant odor and the obscuration of consciousness.

The case to be reported is that of a patient with intracranial disease who for two weeks had a continuous sense of an unpleasant odor; she could find no words to describe it and she could think of no smell with which to compare it. The odor did not come in momentary attacks or in paroxysms, but lasted continuously for two weeks. At no time was there an alteration of consciousness, such as one finds in uncinate gyrus fits. I saw the patient in January 1933. She gave a history of having had parosmic odors for two weeks during the previous summer. When she was seen, not much attention was paid to the symptom. At autopsy a small carcinomatous nodule was found attached to each olfactory bulb. A review of the literature showed that the continuous, nonmomentary, nonparoxysmal type of parosmia due to tumorous involvement of the olfactory bulbs or nerves is rare, and it is for this reason that the case is reported.

REPORT OF CASE

Mrs. G. N., a housewife, aged 45, was first seen on Jan. 25, 1933. At the age of 37 she noticed the presence of a lump in the left breast; at the age of 41 it was found to be carcinoma, and a radical amputation of the breast was performed.

The patient made an uneventful recovery from the operation, and remained in good health until the summer of 1932. When I saw her first, she complained that almost daily for six months she had severe headaches, mostly occipital, sometimes frontal, made worse or brought on by coughing, sneezing or straining and especially made worse by a change of position. Since the onset of the headaches she had suffered a great deal from dizziness, and for the past three weeks had walked on a wide base with a reeling gait and with a tendency to fall to the left.

It was elicited that during the summer of 1932 she had a continuous sense of unpleasant odor for two weeks, and a left homonymous hemianopia for three days.

Read before the Chicago Neurological Society, March 15, 1934.

From the Department of Nervous and Mental Diseases, Northwestern University School of Medicine.

Neurologic examination gave negative results except for the gait; she walked on a wide base and the gait was reeling, with a tendency to fall to the left. She was able to detect in each nostril the smell of common objects, such as tobacco, oranges and bananas. The sense of taste was not examined. The visual fields and the disks were normal, and there was no nystagmus; all other cranial nerve functions were normal. Motion, sensation and reflexes were normal, except that the right knee and ankle jerks were not elicited. There was some incoordination in the knee-to-heel test, but none in the finger-to-nose test.

A diagnosis was made of metastatic carcinoma of the cerebellum. Dr. Loyal Davis performed an operation in January 1933, at which a carcinoma of the left cerebellar lobe was removed, and subsequently roentgenotherapy was instituted.

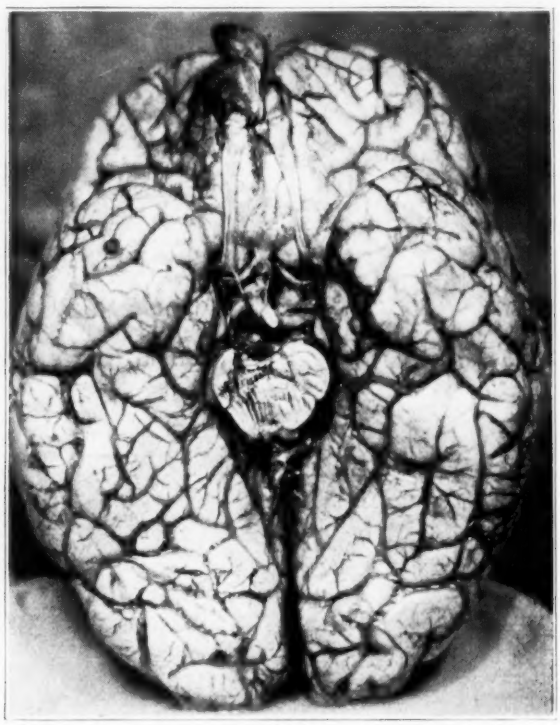


Fig. 1.—Carcinomatous nodule attached to the right olfactory bulb. A similar one was attached to the left bulb, but was torn away in removing the brain.

For a few weeks after the operation the patient's condition was good, but in February she began to fail and died on March 9. Autopsy revealed metastatic carcinoma in the lungs, pleura, peribronchial lymph nodes, various parts of the brain and spinal cord, kidneys, uterus and ovaries. Attached to each olfactory bulb was a carcinomatous nodule about the size of a split pea (fig. 1).

On microscopic study the olfactory nerves and bulbs were found to be invaded with carcinoma cells (fig. 2). In the nerves, some of the fibers were intact; others showed some swelling, and still others were in the early stages of degeneration.

COMMENT

It seems reasonable to believe that the carcinomatous involvement of the olfactory bulbs and nerves was responsible for the unusual type of parosmia with which the patient was afflicted. This type of disorder of smell due to intracranial disease must be rare or has passed unnoticed, or, if noticed, it has not often been reported.

In a thorough search of the literature I have been able to find reports of only a few similar cases: Lockeman [1] reported the continuous presence of parosmia in carcinomatous involvement of the olfactory tract; Wood [2] reported the case of

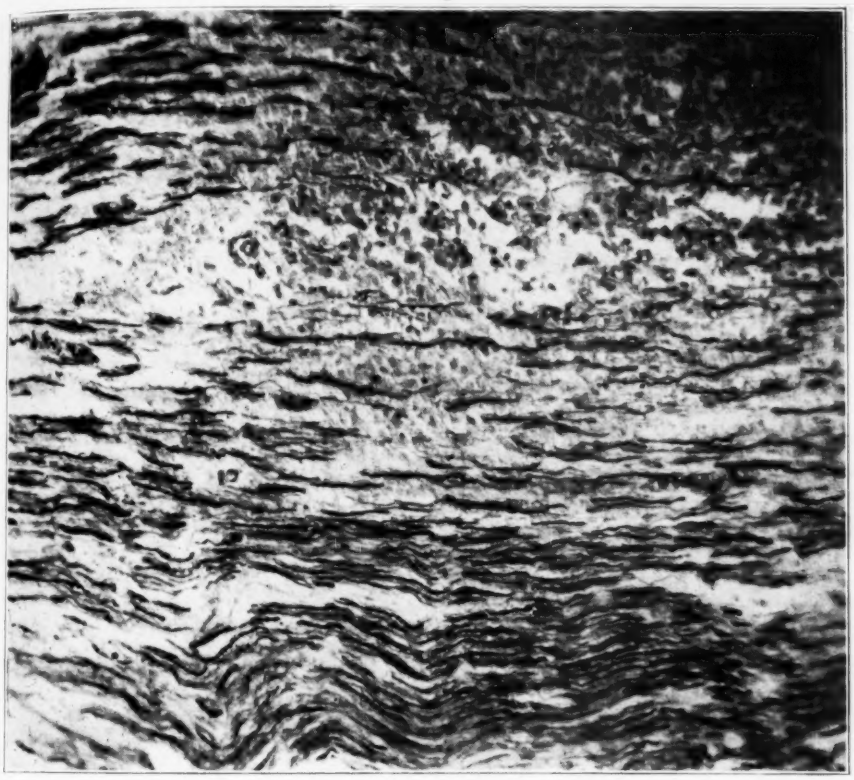


Fig. 2.—The olfactory nerve, with carcinoma cells infiltrating the nerve fibers. Most of the fibers are intact, some are swollen and others in an early stage of degeneration. Davenport stain; × 325.

a patient with a glioma of the frontal lobe, involving the olfactory bulbs, who suffered from a continuous hallucination of disagreeable odor, and Von Frankl-

1. Lockeman: Zur Kasuistik der Geruchanomalien, Ztschr. f. rat. Med. **12:** 340, 1861.

2. Wood, H. C.: Record of Two Cases of Cerebral Disease, Philadelphia M. Times **12:**135, 1881.

Hochwart[3] reported the case of a patient who for days was tormented with horrible smells. At autopsy a fungus of the dura mater (probably a meningioma, in current nomenclature) was found.

There has also been reported the occurrence of continuous parosmic phenomena: in meningitis at the base; in injuries of the frontal fossa; in cerebral arteriosclerosis; in senile changes in the brain; following infectious diseases, especially after influenza, and in infections about the nose and accessory sinuses. These cases, however, are not entirely comparable to mine.

It is difficult to understand why continuous parosmia should be so rare. Anosmia in lesions of the frontal fossa is relatively common; for example, it is frequently observed in meningioma of the olfactory groove. Since anosmia is a symptom of destruction and parosmia a symptom of irritation, it would seem reasonable to believe that parosmia should precede anosmia. That the type of parosmia described here is considered so rare may be due to a failure to elicit a history of it. It would most likely be an early symptom, and may have disappeared by the time the patient appears for examination, where anosmia may be present. It seems, then, worth while to inquire for a preexisting parosmia in cases presenting anosmia.

Parosmia might then be found as an early symptom in intracranial conditions which in later stages show anosmia.

25 East Washington Street.

DISCUSSION

DR. DAVID A. CLEVELAND: I remember this patient in the service of Dr. Davis at Passavant Hospital. When I tested her sense of smell roughly with foods, a piece of soap and tobacco, she recognized those things readily. She tried to describe the peculiar odor more as paralydehyde than anything else.

DR. HARRY A. PASKIND: When I first saw the patient in her home and tested her sense of smell with orange and banana she could recognize them easily. I did not have any of the standard testing materials with me. I saw her six months after the sense of smell disappeared and could find no reaction. She detected no difference in the taste of foods at any time.

---

3. von Frankl-Hochwart, L.: Die nervösen Erkrankungen des Geschmachs und Geruchs, in Nothnagel, H.: Spezielle Pathologie und Therapie, Vienna, A. Hölder, 1898, vol. 2, p. 27.

HUNTINGTON'S CHOREA IN TWINS

AARON J. ROSANOFF, M.D., AND LEVA M. HANDY, M.A., LOS ANGELES

Only a few cases of Huntington's chorea in twins have been reported. Our search through the literature has brought to light reports of only four such cases. In the course of our study of mental disorders in twins a case of this kind was brought to our attention by Dr. George H. Stevenson, superintendent of the Ontario Hospital at Whitby, Canada.

The object of this communication is to review briefly the reports of cases gathered from the literature and to report a new case.

REPORT OF CASES

CASE 1 (Russell,[1] 1894).—*Male twins, probably monozygotic, both affected.*

The father of the twins was choreic as was also probably the paternal grandmother. The twins had three brothers and three sisters (ages not given) who were free from chorea at the time of the report. The chorea developed in both twins at the age of 27 years, occurring a little earlier in one. They were "remarkably alike in appearance," but the movements were less severe in the one with the somewhat later onset. At the time of the report the twins were 34 years of age and had been choreic for seven years. One of them was Dr. Russell's patient in the General Hospital, Birmingham, England. The other was a patient of Dr. Douglas Stanley.

CASE 2 (Kalkhof and Ranke,[2] 1913).—*Opposite-sex, dizygotic twins, the male alone affected.*

The father had been choreic from the age of 40 years and died at 54. One brother had been choreic from the age of 40 years and died at 52. One sister had become choreic at 39 years; she was living and choreic at the age of 43 at the time of the report. Eleven other brothers and sisters, including a pair of twin girls, died in infancy or in early childhood. The twins were born on Aug. 22, 1873. Chorea developed in Josef H., the male twin, in 1908, i. e., at the age of 35 years. The condition grew worse gradually until he was no longer able to work and was admitted to the Bürger Hospital in Colmar, i. e., on April 26, 1911. Mental deterioration was also observed. The twin sister, Josefine, was married, and without children, at the time of the observation (1911) and was free from chorea.

CASE 3 (Owensby,[3] 1926).—*Opposite-sex, dizygotic twins, both affected.*

On the paternal side one great-grandfather, the grandfather, one uncle, one aunt and the patient's father were choreic. No chorea existed on the maternal side. The twins had four sisters, three older and one younger than themselves;

1. Russell, J. W.: Two Cases of Hereditary Chorea Occurring in Twins, Birmingham M. Rev. **35**:31 (Jan.) 1894.

2. Kalkhof, J., and Ranke, O.: Eine neue Chorea-Huntington-Familie, Ztschr. f. d. ges. Neurol. u. Psychiat. **17**:256, 1913.

3. Owensby, N. M.: Huntington's Chorea in a Twin Child, J. Nerv. & Ment. Dis. **61**:466 (May) 1925; personal communication to the author in November 1934.

all were free from chorea at the time of the report in 1925. Chorea developed in the girl twin at the age of 4 years. She was observed at the Good Samaritan Clinic in Atlanta, Ga., at the age of 7 years, when the choreic manifestations were fully developed. Her twin brother was free from chorea at that time. In a recent personal communication the author has reported that the girl died at the age of 9 years of "hypostatic pneumonia in the terminal stage of the disease." Two years later her twin brother, then aged 11 years, also presented chorea and is now (November 1934, i. e., at the age of 16 years) "in a pitiable state of dementia and marked choreiform movements which have made him bedridden; apparently the end is approaching."

CASE 4 (Popenoe and Brousseau,[4] 1930).—*Male twins, monozygotic, both affected.*

The report is brief, stating merely that the twins were identical and were 60 years of age; both had Huntington's chorea and had been under observation together as inmates of the state hospital at Yankton, S. D.

CASE 5.—*Female twins, monozygotic, both affected.*

The S. (maiden name) twins, Rosetta and Rhoda, were born in Lindsay, Ontario, Canada, on Feb. 15, 1877. The paternal grandfather, the father and an older sister died of chorea. At least one other sister and several nieces are also choreic. The twins are described as being so similar in features, build, etc., that "they could not be told apart and their records became very much mixed." The chorea began in both at the age of 35 years and was complicated at first with behavior difficulty and later with psychotic trouble and mental deterioration. Rosetta was first brought to the attention of the authorities in 1915, when she was charged in the juvenile court with gross brutality to her children; Rhoda was brought into the courts for bigamy. On account of the chorea and the obvious mental complications they were sent for observation to the Psychiatric Hospital in Toronto. On May 21, 1918, Rosetta was committed to the Ontario State Hospital at Toronto, from which she was transferred to the Ontario Hospital at Cobourg on Feb. 2, 1923. There she died on Oct. 28, 1931. On May 25, 1918, Rhoda, too, was committed to the Ontario Hospital at Toronto. She was released to the custody of relatives in September 1918, but soon was in difficulty again and had to be placed in "The Haven," a home for "fallen women." From there she was readmitted to the Ontario Hospital at Whitby on Jan. 22, 1924. She remained in this last institution until death on Feb. 17, 1930. Both twins had shown characteristic mental deterioration and also increasing physical disability due to the progressive aggravation of the chorea.

SUMMARY

The cases of five pairs of twins with Huntington's chorea are briefly described. The reports of four were gathered from the literature, and one is a new case.

Three of the pairs of twins were probably monozygotic—two male and one female. In each of these pairs both twins were choreic.

The remaining two pairs were dizygotic, opposite-sex twins. In one of these pairs both twins were choreic. In the other pair only one of the twins—the male—was choreic.

4. Popenoe, P., and Brousseau, K.: Huntington's Chorea, J. Heredity **21**:113 (March) 1930.

While this material is meager in amount, it tends to confirm, as far as it goes, the view of the strictly hereditary etiology of Huntington's chorea.

This is not intended to imply that the syndrome of chronic chorea is always of hereditary origin. Such syndromes have been amply shown by Lannois,[5] Wollenberg,[6] Entres [7] and others as occurring at times in the absence of demonstrable hereditary factors on an infectious, traumatic or arteriosclerotic basis; also there seem to be cases, clinically indistinguishable from true Huntington's chorea, which are of obscure or unknown etiology.

---

5. Lannois: Classification des chorées arhythmiques, Rev. neurol. **3**:66, 1895.

6. Wollenberg, R.: Zur Lehre von der Chorea, Arch. f. Psychiat. **30**:676, 1898.

7. Entres, J. L.: Zur Klinik und Vererbung der Huntingtonschen Chorea, Berlin, Julius Springer, 1921.

SPECIAL ARTICLES

WILHELM HEINRICH ERB
1840–1921

ARNE TORKILDSEN, M.D.
AND
THEODORE ERICKSON, M.D.
MONTREAL, CANADA

From a forester's hut in the Black Forest to the chair of neurology in Heidelberg is a long path but one which Wilhelm Erb plodded with taciturn brilliance to become finally one of the greatest of clinical neurologists. He was born in Winnweiler, Bayerische Pfalz, on Nov. 30, 1840. Of his antecedents nothing is known except that his father was a woodsman. His boyhood was obscure and, as far as is known, uneventful. Erb was not the man to entertain his friends with anecdotes of his early life.

As a medical student at Heidelberg, where he entered the university at the early age of 17, he already showed promise. In his early years he was a serious, hard-working student who took little interest in life outside of his work. In 1864, at the age of 24, he published his first paper, "Picric Acid: Its Physiological and Therapeutic Action," and in the following year, "The Development of the Red Blood Cells." His early studies were all in the field of pathology and internal medicine. His early association with Friedreich in 1867, however, was the dominating influence of his medical life. Of Erb's two hundred and thirty-seven publications, three fourths deal with neurologic problems. Erb owed much to Friedreich as a teacher, for he, more than any other, taught him the value of combining anatomic and pathologic knowledge with clinical observations.

In 1867 appeared Erb's first publication dealing with the peripheral nervous system, "The Pathology and Pathological Anatomy of Peripheral Paralysis," and throughout the rest of his life this part of the nervous system maintained a central position in his wide field of interests.

Erb was already widely known as a scientist when, in 1874 and 1876, he published his two fundamental contributions, "Diseases of the Peripheral Cerebrospinal Nerves" and "Handbook of Diseases of the Spinal Cord and Medulla." These works contained an excellent pres-

entation of the knowledge of that time, and their success was proved by the fact that the second editions appeared shortly after the first.

Electrodiagnostic and electrotherapeutic measures were at this time recent acquisitions to medical knowledge, and Erb was one of the pioneers in their development and application. He has forever associated his name with the reaction of degeneration. In 1882 he published the comprehensive "Handbook of Electrotherapy." He believed implicitly in the curative possibilities of electric currents, as his contemporary Charcot did in the possibilities of hypnosis. He was deeply disappointed when he later realized that mental disturbances could not be cured by electrotherapy.

To the knowledge of musclar atrophies and muscular dystrophies Erb made one of his most valuable contributions, and his theories are discussed to this day. His clinical and pathologic publications, "A Peculiar Bulbar Symptom Complex," in 1879 and "A Juvenile Form of Progressive Muscular Atrophy,"[1] in 1884, are of great scientific value, as is also his study on "Myotonia Congenita," which he presented at the University of Heidelberg on its five hundredth anniversary in 1886. He always remained of the opinion that in the apparently "primary" muscular dystrophies no primary alteration of the muscles is necessary but that the disease is caused by a trophoneurotic condition.

Long before the etiology of tabes was demonstrated in the laboratory Erb maintained its syphilitic nosology from clinical and statistical study. Nonne, who was his assistant in 1885, recalled that Erb's belief in the syphilitic origin of tabes could not be shaken. One day he said to Nonne: "Yesterday there was a tabetic in my clinic. He came from Leyden in Berlin and had been directed to Rome for the winter. I said to him that he might go to Rome if he would get his inunctions there." This belief is all the more significant when one recalls that it was not until 1905 that Schaudinn discovered Treponema pallidum and not until 1906 that Wassermann devised the serologic reaction. Erb was a man of rare and astute clinical insight who made advances in neurology on the clinical rather than on the laboratory front.

During the last years of his life he took great interest in the administration and arrangement of the curricula of medical schools, with special regard to their neurologic and neuropathologic sections ("Neurological Instruction in Our Universities," 1909). In 1914 he came back to this problem, which apparently rested close to his heart, in a paper entitled "What We Strive For." Fate made this publication Erb's swansong, as it was accompanied by the drums of the Great War, and the realization of his ideas concerning medical education was thus prevented even in Heidelberg.

---

1. Erb, W. H.: Deutsches Arch. f. klin. Med. **34**:467, 1883-1884.

Erb, together with Schultze, was editor of the *Deutsche Zeitschrift für Nervenheilkunde"* from the time of its foundation, and he wrote the first article in the first number of this journal in 1891. When the Society of German Neurologists was formed, he became its first president in 1907, and later he was made honorary president. A medal was established to be given at successive meetings in honor of Erb.

He took great interest in administrative work of medical and of local political nature. At the university his work as a teacher interested him most of all. From 1865 to 1880 he was docent and "Ausserordentlicher Professor" in Heidelberg, and in 1880 he became Friedreich's successor

WILHELM HEINRICH ERB
1840-1921

in Heidelberg, where he worked until his retirement in 1907. In manner he was brusk, and in temperament, intense, and he offended many by his use of language unusual in academic circles. He was gruff to all and prone to lose his temper. Hence he was more respected than loved by most of those who worked with him. He demanded as much from his associates as from himself. However, those who knew him well said that beneath this rough exterior he was kindly and that he never neglected an opportunity to do a kind and thoughtful deed.

At the height of his career he was internationally known, not only as a scientist but also as a practitioner, and he was extensively called on

as a consultant. In his waiting-room could be seen, side by side, aristocrat and peasant, both of whom Erb treated as equals, with the same sincere wish to help the one as the other.

Unlike so many great men, Erb received in his own country, as well as in his own time, the acknowledgment which his work deserved. He was recognized as a great scientist and a celebrated man, and from his Grand Duke he received the title of Excellency. On his seventieth birthday a bronze statue of Wilhelm Erb was unveiled in the park of Das Akademische Krankenhaus, and a street of Heidelberg was named in his honor. But his life with its many triumphs also brought him much grief and sorrow. His work was frequently interrupted by illness. For many years he suffered from a cardiac neurosis with tachycardia and arrhythmia. For a long time also he suffered from gallstones, a condition which was relieved only after a serious operation. Apart from these conditions, he led a healthy life and had until death a florid complexion and an apparently sound constitution.

It is true that this tremendous worker each year took a long summer holiday, but he usually returned with one or more manuscripts ready for publication. A forester's son, he always derived great pleasure from nature and outdoor life. He spent most of his vacations in the Black Forest, but he was fond also of attending international medical meetings during his holidays.

Of his four sons, two died in adult life, one a physician. Then came the Great War, and for the old man of almost 80 the ruin of the fatherland he loved was almost more than could be borne. When one day from the western front he received the tragic news of the death of another son, a hero of the war, his grief was profound. After this shock he never regained his desire to live. An intestinal infection broke down his strength, and one day while attending a concert and listening to his favorite symphony, Beethoven's "Eroica," he had an attack of syncope which gradually passed into a calm and peaceful death on Oct. 29, 1921.

Erb has claim to greatness because of a multitude of contributions to the science of clinical neurology. The very foundation of neurology, the neurologic examination, owes much of its origin to him. Simultaneously with Westphal [2] he discovered the importance of the pupillary reactions and the tendon reflexes. In his clinical examinations he was thorough and always emphasized the importance of these reactions.

The interpretation of these simple fundamental reflexes was perhaps his greatest contribution to the development of neurology. He also introduced in 1868 the methods of electrodiagnosis by the use of galvanic and faradic currents. He described many new syndromes. In

2. Westphal: Arch. f. Psych. u. Neurol. **5**:792, 1875.

1874 he described brachial palsy; in 1875, syphilitic spinal paralysis; in 1884, the juvenile type of muscular atrophy, and in 1878, myasthenia gravis. Erb gave the first description and classification of the muscular atrophies (1891) and did much to establish the modern theories concerning their pathogenesis. With his astute clinical sense he recognized the syphilitic origin of tabes long before it was proved in the laboratory. He was a leader in the development of neurology as a medical specialty and in the establishment of proper neurologic instruction and research in the universities.

Erb's fame was made possible by hard work over a long period of time, with close attention to detail. His thorough and painstaking examination of patients was exemplary. All the results of his work he imparted to a host of students and associates who have transformed it into a portion of the neurologic tradition of today.

FRANZ NISSL
1860–1918

ALOIS ALZHEIMER
1864–1915

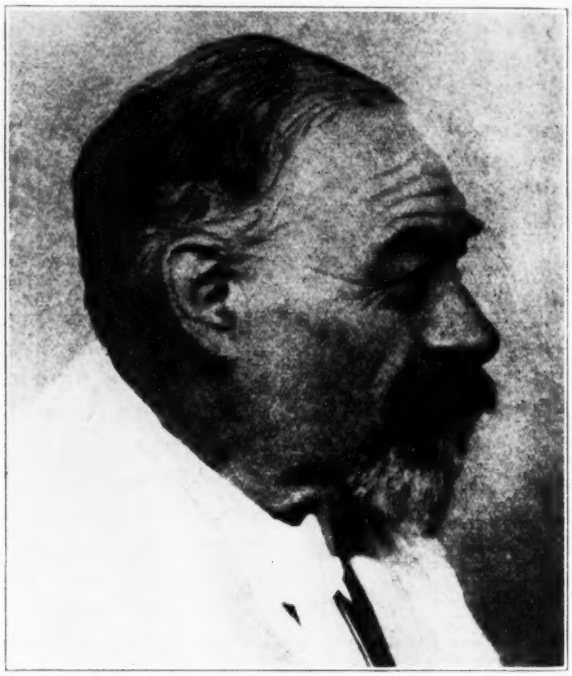
ARTHUR W. YOUNG, M.D.
MONTREAL, CANADA

In reviewing the history of medicine, one is struck by the fact that whenever ignorance and confusion dominate a particular field of medical knowledge nature seems to concentrate in one or two men great forces of intellect to penetrate the darkness and discern in the dimness of half-knowledge shining principles of truth. The greater the need, the greater the effort nature makes to create adequate response. She fashioned powerful minds to cope with superstition and mystery in the early centuries and to overcome medieval blindness. Approaching recent times one sees nature again at work, meeting great demands in the domain of surgery and medicine with the fine minds of the medical profession in the past century, and the crying need for advance in the knowledge of the histology of the nervous system finding a glorious answer in the work of Alzheimer and Nissl.

To these two scientists mankind owes a deeper and better understanding of diseases of the mind, a clearer definition of the demarcation between the types and a surer concept of the histologic changes. Cerebral architecture as regards cellular response to disease owes to them in great part its clarity of definition. Working hand in hand in the latter part of the nineteenth and in the twentieth century, they brought to the problems of pathologic changes of the cerebral cortex the combined forces of great intellect and the unceasing will to work. Interested especially in the organic changes in mental disorders, they attempted to link the clinical to the anatomic picture. It was their cherished hope that specific processes would be identified by a particular type of change in the ganglion cell. This theory led them to give detailed and accurate histologic descriptions, but in the final analysis they were forced to the realization that alterations in cellular structure were not specific and did not portray even the chronicity of the process.

Franz Nissl, born in Frankenthal in 1860, made his first contribution to scientific knowledge at the age of 24, when he presented a thesis entitled "The Pathological Changes of the Nerve Cells of the Cerebral

Cortex." For this thesis he was awarded a prize by the University of Munich. The young student was greatly stimulated by the recognition of the university and threw himself with all the enthusiasm of youth into the work of investigating, revising and perfecting methods of study which in the domain of histopathology were at that time archaic and without precision. Indebted as neurology is to Golgi and Cajal for descriptions of the projections of the ganglion cells and the intracellular network, it was the labors of Nissl which led to the adoption of alcohol as a fixative and aniline dyes as stains. His method gave clear, simple



FRANZ NISSL
1860-1918

and constant pictures of the chromidial structure of the cytoplasm, and both the toluidine blue stain and the chromophilic bodies carry his name.

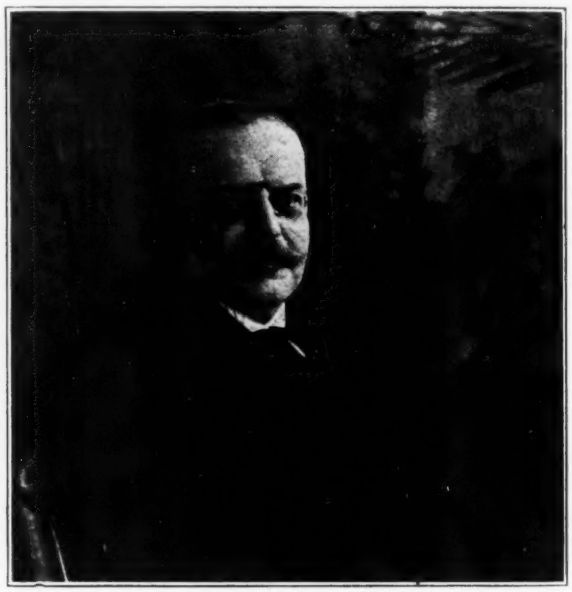
He brought to his work the freshness of vision of a young man combined with mature judgment. He brought as well high ethical standards, for he had originally been intended for the clergy. He possessed, too, a character already inured to hardship, for he had achieved his medical training only after difficulty and perseverance. The worth of the young man was soon recognized by Gudden, and in spite of

his youth he was made assistant in the district hospital for patients with mental disease in Munich. There he carried on his pathologic research, interesting himself particularly in the normal histologic structure of the cerebral cortex, aware that a thorough understanding of the ganglion cell and its background was necessary if pathologic alterations were to be correctly interpreted. For three years he carried on his work with Gudden, frequently asking for the assistance of others in his search for truth, for with the humility of the truly great he was never puffed up with the importance of his own contributions. Unfortunately, his activities were interrupted by the renal trouble which throughout his life was to prove a source of great suffering and inconvenience. Nissl, however, was not the man to capitulate in the face of illness, and a few months later he was again at work, this time at the state hospital at Blankenheim. His stay there was short, for he was soon appointed second physician at the state hospital at Frankfurt.

There, in 1889, he found Alois Alzheimer, a man of 25, of French birth, who was fired with an enthusiasm for research akin to his own. It is not difficult to understand the stimulation and comradeship which these two men found in each other and which formed the basis of a long and close association between them—an association outstanding in medical history on account of the character of the men and the quality of their achievements. Over a period of nearly twenty-five years, now separately, now together, they carried on their work of investigation and correlation. Nissl, with his stupendous powers of intellect and imagination, turned to more general questions, whereas Alzheimer, an analytic, remarkable and reliable observer, made important pathologic and anatomic observations. Picture these men after a strenuous day working far into the night in a small laboratory with few facilities, and their observations become even more remarkable. An idea of their influence on neuropsychiatry in Europe and abroad and of the breadth of their work can be obtained from the "Histologische und histopathologische Arbeiten über die Grosshirnrinde" (1904-1918), six beautifully edited volumes which contain Nissl's careful analysis of dementia paralytica and Alzheimer's conception of neuroglia, as well as other articles by themselves and their postgraduate students, most of whom have advanced to fame.

Alzheimer crystallized, after years of labor, descriptions of many pathologic changes of the cerebral cortex. To him neurology is indebted for the description of the disease which bears his name, typified on the pathologic side by senile plaques scattered throughout the cerebral cortex, profound changes of the intracellular fibrils, fragmentation, thickening, club formation and destruction of the nerve fibers and moderate vascular proliferation. Kraepelin was the first to credit him with the elucidation of this state, which begins in middle life or a little

later and clinically is characterized by defects in memory, progressive dementia, apraxia, aphasia, confusion and paralysis. Indeed, this man, with inexhaustible enthusiasm and unfailing insight, threw the searchlight of investigation in all directions, to uncover truths unbelievable in range and truly lasting in value. He recognized in dementia praecox (1897) a dropping out of cells limited to one cell layer or another, degeneration of the cell body and nucleus, regressive pigmentary changes and glial bands. He assumed that disturbance of cerebral function was the result of changes in the ganglion cells and their end-processes, and although dementia praecox has since proved a provocative field for



ALOIS ALZHEIMER
1864–1915

pathologic research, little has been added to his original observations. He recognized acute and chronic changes of the ganglion cells in various psychotic states, but when he attempted to correlate and sum up his observations, to his dismay a lack of specificity was evident. He gave, however, a clear description of some of the mental disorders of organic origin, occupying himself especially with arteriosclerotic changes of the brain in dementia and paralysis, interpreting presenile and senile paralysis on a pathologic basis and, with Nissl, giving the first exact pathologic picture of dementia paralytica. But the versatile brain of Alzheimer was not satisfied with consideration of pathologic alterations; he turned as well to the fascinating problem of unraveling the com-

plexities of psychiatric states. He early found that the clinical methods used in deciphering problems in other branches of medicine were of little value in these conditions, and after much deliberation he came to the realization that all reactions of the particular types were influenced by hereditary, environmental, endogenous and exogenous factors.

Meanwhile, Nissl first described the rod cell in dementia paralytica, an "extraordinary long cell, whose cell body does not appear plainly or adheres to both poles in the form of a single thread." He advanced the theory of the hematogenous origin of the reactionary cells in the perivascular spaces and the transition of lymphocytes into plasma cells and mast cells.

The association between Alzheimer and Nissl, so happily begun in Frankfurt, was interrupted after six years when Nissl was called to Kraepelin's clinic at Heidelberg. The association was resumed in 1903 when Alzheimer also came to Heidelberg.

Kraepelin testified to the high character of Nissl when he said in the obituary:

> He possessed a thoroughness in research which was stopped by no obstacles, by no difficulty, but, above all, an almost cruel self-criticism which could not be corrupted and which controlled all his thinking, and a boundless caution in regard to all conclusions. Because of this he could hardly do enough to satisfy himself in objections, reservations and oft-repeated testings. Therefore the exceptional trustworthiness of his statements, which assured him the unconditional confidence of his fellow-workers.

Not only did he inspire confidence, but he was beloved by all—students, fellow workers and patients. He was as tireless in his investigations in the clinical as in the anatomic field. In love with truth and with deep reverence for things truly great and beautiful, he discarded pettiness and made no concession to meanness or smallness of any kind. The serious side of life claimed his attention, although he enjoyed communion with nature and the company of children. He never married.

Nissl continued his searching studies while in Heidelberg and won his degree with a study on chronic diseases of the cell; at the same time he completed his book, "The Neurone Theory and Its Adherents." By animal experimentation he showed the effect of different toxins on nerve cells and established the fact that sometimes the reactions were distinctive. He made important observations on the cerebrospinal fluid in respect to cellular reaction and quantitative determinations of albumin. He became adjunct professor and later professor of psychiatry and director of the psychiatric university clinic at Heidelberg. In 1910, worn out with the multiple demands of his office and once more overcome by illness, he was forced to spend the winter in Egypt. This, however, was not an unmitigated hardship, for he had ever found

constant delight in travel. Returning to his post, though hampered by ill health, he resumed his work of investigation and correlation and was honored by being made director (a purely scientific post) of the newly founded institute for research at Munich in 1918.

He was in the midst of presenting the relationship of the thalamic nuclei and cortex, which he had mapped out after much investigation and animal experimentation, and was interesting himself in the relationship of one cortical field to another when his labors were interrupted. The renal trouble which had haunted him all his life claimed him, and he died on Aug. 11, 1918, at the age of 58. Contemplating his death in the midst of unfinished work, one is tempted to quote these lines by Dehmal:

> The moment comes when, before I shall have finished reading,
> The scroll slips from my exhausted fingers,
> And with fettered hands you leave it to the winds to say
> What I have done.

In Kraepelin's clinic at Heidelberg Alzheimer also distinguished himself by the purity of his strivings, and his genius was recognized by his being made professor of psychiatry at Munich and in 1912 professor of psychiatry at Breslau. Inexhaustible vitality, untiring activity and a tenacious and firm belief in observations activated his work, and with the passing of years his energies gathered momentum and he published the results of his earlier experience, writing on such subjects as the theory of epilepsy, diagnostic difficulties in psychiatry, chorea and senile diseases.

During all his studies on the cerebral cortex he never lost himself in the maze but could always foresee the step ahead. The life work of Alzheimer was so great that it constitutes a living picture of his personality. He was a clear-headed scientist who knew where research was needed and where it was most profitable. Confidence and self-criticism marked his work. Every one who knew him felt the gentleness, the kindness and the spirited force of the founder of the *Zeitschrift für die gesamte Neurologie und Psychiatrie,* an everlasting memorial to this man of genius. He died at Breslau in 1915 at the age of 51.

Intimately associated in life, Nissl and Alzheimer died within a short time of each other, and as witness to the real union between them Gaupp wrote: "What I wrote three and a half years ago at the death of Alzheimer I should like to repeat today at the grave of his, and our, near friend, Nissl. Our life is poorer and it became colder around us when we saw him depart. We have loved him too much to forget him."

Abstracts from Current Literature

HISTOPATHOLOGY OF CONGENITAL MYXEDEMA. G. MARINESCO, Jahrb. f. Psychiat. u. Neurol. **51**:108, 1934.

A patient with typical congenital myxedema, a youth, aged 19, came under Marinesco's observation three days before death. All that is known about the patient's previous history is that he had had myxedema since birth and showed evidences of physical maldevelopment and amentia. He never spoke.

Gross examination of the brain revealed no striking abnormalities. Histologic examination disclosed a diminution in the size of all cells and of their nuclei and nucleoli throughout the entire cerebral cortex and a diminution in the number of dendrites. The cells in other regions of the neuraxis (the cells in the nuclei of the thalamus, bulb and basal ganglia, the Purkinje cells and even the cells in the spinal ganglia) were also small. Besides the diminution in size, the cells in the cortex throughout the second and third layers showed poorly differentiated Nissl bodies. The radial fibers were diminished in number and much shorter than normal. These changes are similar to those reported by Pietro Rondoni, who after examining Brodmann's area 4 in many cases of idiocy concluded that in these pathologic states there is an arrested development of the pyramidal supragranular cells; the arrested development of these cells explains the poor development of the Kaes-Bechterew fibers.

According to Marinesco, these findings in an actual case of myxedematous idiocy confirm his previous researches in which he showed that the retardation of the psychic functions in this disease is in direct proportion to the arrested development of the cortical cells and their dendrites.

Examination of the muscles showed some of them affected with a type of myopathy characterized by changes in the fine structure of the muscular fibers, diminution of the oxydases, increase of lipoids as a result of mitochondrial disintegration, inequality of the size of the muscle fibers, polychromatophilia and atypical circular fibers around the long fibers, as described by Scriban and Bacaloglu. The significance of these circular fibers has not as yet been determined, but they are believed to be an expression of arrested or retarded development of muscle fibers. These primary myopathic changes were not found in all muscles, nor did they involve an entire muscle; they were usually found only in certain portions of a muscle.

The suprarenals showed a diminution in the quantity of lipoids in the fascicular zone and the presence of lipoidophilic histiocytes in the region between the acini and the reticular zone.

The hypophysis showed characteristic changes. First, the entire architecture of the gland seemed to have been destroyed. The glandular acini consisted of three kinds of cells: (1) numerous small chromophobe cells, some of which were rich in chromatin and others of which had a large vesicular nucleus; (2) cells with hypertrophied basophilic granules, which also formed a considerable part of the structure of the hypophysis (these appeared in the form of streaks or heaps, occupying especially the central part of the anterior lobe), and (3) less numerous eosinophilic cells scattered diffusely among the chromophobe cells. The granules of these cells were not always visible; they were unequal in size, and the colloid in them was not always demonstrable. Throughout all preparations stained with hematoxylin and eosin there were observed cells the diameter of which varied between 6 and 60 microns with a concentric structure the center of which appeared more distinct with the eosin stain, and the periphery more distinct with the hematoxylin stain.

In the liver the Kupffer cells generally contained no lipoid, and there were also observed swollen cells loaded with iron, especially in areas in which the hepatic cells were free from fat, although most of the cells contained fat.

The kidneys showed, at the level of the straight tubules, globules of varying size and masses staining dark red with hematoxylin; between these masses there were some which showed a reaction to iron. Some of the straight tubules also showed a crystalline substance which did not stain with hematoxylin.

The testes were hypogenetic and of the fetal type and contained small and large germinative cells and a number of interstitial cells which appeared atrophic. The seminal tubes were much smaller than one would expect at the age of 19.

Following the description of the histologic picture in the viscera and the central nervous system, Marinesco discusses the physiologic mechanism of the lesions in congenital myxedema. He points out that one of the striking features of this condition is that the morphologic changes produce a diminution in the volume and weight of the cells of the viscera and of the central nervous system. This diminution in volume and weight is, to a certain extent, systematic and proportionate to the course of development of the different nerve centers, affecting especially those that attain their definite organization rather slowly. This accounts for the fact that the cells in the roots of the spinal cord and of the bulb are less affected than the Betz cells, whereas the association elements, especially in the subgranular layer of the neopallium, are most affected by the absence of thyroid secretion. Normal development of the neurons and their projections is compatible with an optimum temperature of about 37 C. (98.6 F.) as maintained by an active thyroid gland. The absence of this gland produces a diminution of the intensity of oxidation and affects secondarily thermogenesis, because in the final analysis all biologic phenomena as well as chemical reactions are affected by changes in temperature.

Experimental and clinical data prove that the thyroid gland plays an important rôle in regulating body temperature. Clinico-anatomic investigations of myxedema confirm this, because it is well known that myxedematous persons are unable to tolerate low temperature and always show some hypothermia. It is this hypothermia which, Marinesco believes, accounts for the nutritional changes, diminished energy and failure of normal development.

To understand the physiologic mechanism of the lesions in the nervous system and in the other organs in cases of myxedema it is necessary to recall the significance of the thyroid gland for normal morphologic, trophic and catabolic functioning. The principal function of the thyroid is to accelerate and maintain oxidation and consequently the body temperature at a constant level. The control of the metabolism of calcium and other ions, as well as of carbohydrates, depends on the maintenance of a constant level of oxidation. One may say that human beings as well as other mammals deprived of the thyroid body behave in the same fashion as heterothermic animals.

The administration of a small quantity of thyroid to young animals enhances their development. Schaffer has shown that the ingestion of a small amount of thyroid improves the appetite, especially in small animals; development is accelerated, and there occurs a retention of nitrogen in the organism, at the same time that the nitrogen metabolism as well as the excretion of phosphorus, lime and magnesium is greatly increased.

Heat is an essential stimulus to protoplasmic activity and promotes the release of all potential energy necessary for development and for the maintenance of all processes of life. In the same cell there exist various elements (proteins, fats and carbohydrates), each of which corresponds to a soluble ferment the activity of which exercises in a sense the same function as temperature. Patients with congenital myxedema generally have a temperature from 2 to 2.5 C. (3.6 to 4.5 F.) below normal, which not only retards the activity but diminishes the quantity of the ferments. In the case under discussion, as in animals deprived of the thyroid, the quantity of oxidizing ferments in the viscera was markedly diminished.

The stimulating effect of the thyroid gland on the development of the nervous system, according to Marinesco, has recently been studied by Champy, who found that in tadpoles fed with thyroid for from two to five days there was an increase in mitosis of cells which, though present in the entire brain, was much more active in the cerebral periependyma. Finally, Marinesco quotes Hammett, who performed

thyroparathyroidectomy to determine its effect on the development of the brain and spinal cord of albino rats varying in age from 100 to 150 days. Hammett concluded that ablation of the thyroid gland is followed by considerable retardation of development of the brain and cord. This phenomenon was more marked in female rats and affected the brain more than the cord, whereas ablation of the parathyroid gland had a minimal affect on the development of the nerve centers. The cause of the retardation of the development of the brain as contrasted with the development of the cord depends, according to Hammett, on the lesser developmental capacity of the latter, on account of the greater quantity of proteins and lesser quantity of lipoids in the brain in contrast with the greater quantity of lipoids and lesser quantity of proteins in the spinal cord. It seems that the formation and storage of lipoids in the cells depends less on the anabolic function of the thyroid than on the active material which constitutes the cytoplasm. The presence of glycogen in the ganglia, radicular cells, bulbar nuclei, olives, etc., is so rare that its occurrence has not been mentioned in myxedema and rarely, with the exception of diabetes, in other disturbances of the central nervous system.

KESCHNER, New York.

VALLECULAR DYSPHAGIA. JOHN E. MCGIBBON and J. H. MATHER, Brit. M. J. **2**:1013 (Dec. 2) 1933.

Elucidation of the causes of dysphagia arising in the lower part of the pharynx has always presented difficulty. Gross neoplastic and ulcerative lesions can be recognized with the laryngoscope, but there have remained a large number of undiagnosed cases in which the condition has been termed "functional dysphagia" and "globus hystericus." The authors were stimulated by the report of a case by Dr. R. R. Woods in which the difficulty in swallowing was designated as vallecular dysphagia. They have observed fourteen cases of what they term primary vallecular dysphagia and a considerable number of cases which they classify as instances of secondary vallecular dysphagia.

The valleculae are two fossae situated in the anterior aspect of the lower part of the pharynx, between the pharyngeal portion of the tongue and the epiglottis. They are bounded anteriorly by the base of the tongue and laterally by ridges of mucous membrane—the pharyngo-epiglottic folds. They are separated from each other by the glosso-epiglottic fold. The floor of the valleculae lies immediately above and behind the hyoid bone. They vary much in depth in different persons. Their sensory nerve supply is derived from the glossopharyngeal and superior laryngeal nerves. Deglutition is a complicated reflex act. The afferent nerves are the second division of the fifth nerve, the ninth nerve and the pharyngeal branches of the superior laryngeal nerves. The efferent nerves are the third division of the fifth nerve and the seventh, ninth, tenth, eleventh and twelfth cranial nerves. The center is situated in the medulla and may be considered as a chain of associated centers, stimulation of one of which fires off the others in orderly sequence. The revised concept of the mechanism of swallowing is described, and the older explanation that the bolus of food is seized by the pharyngeal constrictors and forced into the esophagus, where it is passed on by peristalsis, is disproved; it seems that the passage of food through the lower part of the pharynx and upper part of the esophagus is accomplished by a combination of propulsion and negative pressure.

Careful screen examinations of the act of swallowing in more than one hundred normal men and women were made. In approximately 50 per cent of the cases the bolus of food was swallowed, leaving only a trace in the mouth and pharynx, none being seen to enter the valleculae. In the other 50 per cent, a little opaque material entered the valleculae but was evacuated almost immediately by their compression during the succeeding acts of swallowing.

Of the authors' fourteen cases of primary vallecular dysphagia, five were in females and nine in males. The usual complaint was discomfort on and after swallowing, which was referred to the region of the hyoid bone and had been present for from fourteen days to about two years. In some cases the discomfort

was intermittent and occasionally persisted for some time after eating. In some cases the onset was insidious, and in others it was sudden. None of the patients complained of dyspnea or such marked symptoms as occurred in the case reported by Woods. Indirect laryngoscopic examination revealed the presence of food in the valleculae in only one case. Roentgenographic investigation showed that when patients were told to swallow repeated attempts to do so were ineffectual in passing the bolus of food from the mouth into the pharynx. At each attempt a little food passed (1) into the valleculae, (2) into the right and left pyriform fossae and (3) into the pharynx and esophagus. General clinical examination in these cases revealed no systemic disease.

In what the authors have termed secondary vallecular dysphagia, the valleculae were filled in a similar manner, but this abnormality was due to a manifest lesion somewhere within the reflex arc or in the pharynx or esophagus itself. The presenting symptoms were those of the primary lesion, and the vallecular filling and retention were discovered only by routine examination, the findings being similar to those in the primary form of dysphagia but less marked. This condition was observed in patients suffering from carcinoma of the esophagus, postcricoid carcinoma and pharyngeal pouch. It occurs in cases of bulbar paralysis, bilateral recurrent nerve paralysis, tabes with paralysis of the vagus, injury to the vagus and botulism following diphtheritic paralysis etc. It appears that it occurs only with lesions of relatively rapid evolution since the neuromuscular apparatus seems to have the ability to accustom itself to abnormal conditions and to overcome the mechanical difficulties present.

The pathologic condition in primary vallecular dysphagia is doubtful, but from what is known of the pathologic process in the secondary form, it seems that there must be somewhere a failure in the neuromuscular mechanism of swallowing. The anterior group of muscles, consisting of the mylohyoid and the geniohyoid muscles, the posterior fibers of the genioglossus muscle and the anterior belly of the digastric muscle, are the most important. This group of muscles pulls the larynx upward and forward behind the base of the tongue and also pulls the larynx forward away from the posterior pharyngeal wall to open up the hypopharynx. With impairment of this forward movement of the larynx, the valleculae can readily fill and are not emptied by compression. It may be, therefore, that there is present some neuromuscular inferiority in this group of muscles which will easily permit its partial or complete dysfunction from nonobvious causes and so give rise to vallecular filling and retention. Diagnosis of the condition can be made only by careful local and general examination, together with thorough roentgenologic investigation. Either examination alone is valueless.

In thirteen of fourteen of the cases of primary vallecular dysphagia, troublesome symptoms disappeared after explanation and reassurance. One patient apparently went from one hospital to another for advice. Frequent gargling with plain water after meals has been recommended, and also repeated drinking of small amounts of water after meals. Removal of the free portion of the epiglottis has been suggested and appears to be a rational mode of treatment if the symptoms are sufficiently severe. In the secondary forms treatment naturally is directed toward the primary lesion.

FERGUSON, Niagara Falls, N. Y.

HYPERPARATHYROIDISM: A CHAPTER IN SUCCESSFUL LABORATORY RESEARCH. EDITORIAL, J. A. M. A. **102**:1764 (May 26) 1934.

A stimulating record of clinical research by Albright, Aub and Bauer on hyperparathyroidism, recently published in *The Journal of the American Medical Association* (**102**:1276 [April 21] 1934), serves as an interesting reminder of how effectively some of the disconcerting manifestations of disease and the "pathologic curiosities" of practical medicine are being explained by improved procedures in laboratories of medicine. To many it may seem strange that in this day "laboratory medicine" needs any apologies or defense. Yet not long ago Mendel (*Science* **76**:393 [Nov. 4] 1932) of Yale University said that there are today not a few

physicians as well as other friends of medicine who, although admitting the noteworthy contributions of animal experimentation, nevertheless urge that its dominant importance is passing. Though the pendulum of enthusiasm for a laboratory innovation may at times swing too far, it soon reaches a stable level. In his defense of scientific experimentation in medicine, Mendel made a vigorous plea that devotees of practical medicine and surgery refrain from unwarranted derogatory attacks on one of the best helps of their profession in the past. It is difficult enough, he added, to fight suffering, disease and death without being obliged to fight the ignorance and prejudices of those who would tie the arms of the laboratory worker. The ultimate objective of all methods of attack on ignorance is the same.

Osteitis fibrosa cystica, commonly called Recklinghausen's disease, has long been recognized as a chronic progressive disease of the skeleton. One will look in vain for any rational or well founded discussion of its etiology and treatment in all except the most recent textbooks, for it was not until the present decade that the relation of the malady to hyperparathyroidism was clearly established through the classic observations of Mandl (*Arch. f. klin. Chir.* **143**:245, 1926) in Vienna and Du Bois and his co-workers (*J. Clin. Investigation* **8**:215 [Feb.] 1930) in New York. Only a few years ago less than one hundred cases of Recklinghausen's disease had been mentioned in medical literature (Locke, E. A., in Cecil: Textbook of Medicine, ed. 2, Philadelphia, W. B. Saunders Company, 1930). The report of Albright, Aub and Bauer presents seventeen proved cases of hyperparathyroidism from a single clinic in the Massachusetts General Hospital in Boston.

What are the main features of the newer knowledge? Foremost is the observation that hyperparathyroidism is usually due to a functioning adenoma of the parathyroid glands. Sometimes there is hyperplasia of all parathyroid tissue. As a result of the increased production of the parathyroid hormone there is a disturbance in the metabolism of calcium and phosphorus. The easily measurable manifestations of this disturbance are an elevated serum calcium level, a lowered serum phosphorus level and an increased excretion of both elements in the urine. The ascertainment of these diagnostic features has depended on the discovery of the endocrine function of the glands involved, on methods for the ready clinical estimation of calcium and phosphorus in readily obtained small specimens of blood and on the unraveling of the fundamental features of replacement therapy and dietary control. Every detail of these highly significant and frequently life-saving factors has emanated from the scientific laboratories through the laborious and modest efforts of persons who are sometimes referred to somewhat disparagingly as "research hounds." One may recall that the epithet "book farmer," similarly applied to progressive students of agriculture a generation ago, has long since been abandoned.

The relations of parathyroid function to calcium and phosphorus may bring the reminder that about 85 per cent of the mineral matter of bone, or at least three fourths of the entire ash of the body, consists of calcium phosphate. Probably more than 99 per cent of the calcium in the body belongs to the bones, the remainder occurring as an essential constituent of the soft tissues and body fluids. That is why any influence such as hyperfunction of the parathyroids with attendant hypercalcemia leads so characteristically to demineralization of the bones. They become porous and filled with osteoclasts. There are drastic secondary consequences. The increased mobilization and excretion of calcium and phosphorus in the urine not infrequently lead to the formation of urinary calculi. In some instances the calcium phosphate precipitates occur in the parenchyma of the kidney and lead to secondary renal contracture and insufficiency (*Am. J. M. Sc.* **187**:49 [Jan.] 1934). Again, the replacement of so much of the marrow cavity with fibrous tissue leads to a decrease in the hematopoietic elements and hence occasionally to anemia and leukopenia.

Despite the fact that the bones are the storehouse for calcium and phosphorus in the body, according to Albright, Aub and Bauer, the teeth do not take part in the generalized decalcification. They may fall out because of disease of the jaws,

but they themselves remain well calcified. This is brought out strikingly by roentgenograms in which the well calcified teeth stand out sharply against the poorly calcified jaws. This failure of the teeth to become decalcified is featured as strong evidence against their containing a reserve supply of calcium.

The management of the parathyroid tumors presents a real challenge to the modern surgeon. As Albright, Aub and Bauer say, before undertaking an operation he must be more than just "a good thyroid surgeon." He should know the normal and possible aberrant situations of the parathyroid glands; he must be familiar with their reddish-brown coloration and smooth surface (in contrast to the granular surface of the thyroid); he must be able to differentiate them from lymph nodes, collections of fetal fat and thyroid lobules, and he must be prepared to continue the search, even if this leads him into the anterior mediastinum. For the latter reason, the surgeon must not undertake the operation until he is convinced by the blood chemistry that a tumor is present. There is no time like that of the initial operation to find the tumor. The hypoparathyroidism following the removal may be dangerous with its attendant tetany. A diet including calcium and phosphorus in abundance may prevent decalcification and thus improve the bones, yet may need to be avoided because of the possibility of renal damage. These features suffice to indicate the acumen and modern knowledge that are requisite for the management of hyperparathyroidism. The Boston investigators stress the point that, whereas the disease can hardly be called common, it must frequently be considered when any of a multiplicity of symptoms is present. Failure to make the diagnosis is regrettable in that the treatment is highly successful.

EDITOR'S ABSTRACT.

REFLEX DYSKINETIC PHENOMENA IN CEREBRAL TRAUMA. GERHART JACOBY, J. f. Psychol. u. Neurol. **46**:1, 1934.

CASE 1.—A man, aged 40, seventeen years following an extensive gunshot wound in the left temporal region, presented the following symptoms and signs: right tonic hemiparesis, bilateral signs referable to the pyramidal tract, right hemianesthesia, dysarthria and paraphasia, a tendency to fall to the right, with deviation and pastpointing of the right upper extremity, Magnus' Stutzreaktion and prolonged reflex muscular contractions in that limb.. No spontaneous dyskinetic phenomena were observed. During repeated attempts to elicit the finger reflexes and on stroking or pricking the skin of the right side of the body there appeared an extension and spreading movement of the fingers which was associated with abduction and extension of the shoulder joint and extension of the knee with dorsiflexion of the foot and toes, all on the right side; all abnormal movements were associated with increased tonicity of synergic muscle groups on the affected side. The movements of the toes and fingers were regular, harmonious and invariably in the same direction; only rarely did they begin with flexion of the hand and fingers which would lead to making a fist; on such occasions it was noted that excessive hypertonicity of the flexors of the forearm preceded the test. In the larger joints (shoulder and knee) the spasticity made its appearance in definite phases, with the result that the abnormal movements of these joints also appeared in "cog-wheel" fashion; when the movements were at their height they were also associated with more or less pronation of the forearm. The abnormal movements in the smaller joints resembled those observed in choreoathetosis, while those in the larger joints reminded one of torsion spasm. The appearance of the movements necessitated a summation of stimuli; when the last phase of the latent period had been reached a continuation of the stimulation produced no gross changes in motility or posture. With the cessation of the stimulus there was spontaneous cessation of the motor phenomena. Analogous reactions were observed during the epileptiform seizures to which the patient was subject; they also appeared during the initial stages of the convulsions and during one jacksonian seizure, so that suspicions were aroused lest they were epileptogenic irritative phenomena which could be elicited by sensory stimulation. Stimulation of the left half of the body by stroking or pricking the skin produced no abnormal motor reactions.

Jacoby attributes the hemiparesis, hemihypesthesia and disturbance of speech to severe damage of the cortex in the precentral and postcentral convolutions, as evidenced by the extent and depth of the defect in the skull; the homolateral signs referable to the pyramidal tract also indicate involvement of the contralateral pyramidal tract, either by contrecoup or as a remote effect. The tonic phenomena, he believes, are due to a lesion in the midbrain, especially in the region of the red nucleus and in the substantia nigra. The peculiar systematic athetoid movements, with the exquisite extensor movements following sensory stimulation, have for their anatomic substratum a similar localization in the mesencephalon. The disturbances in equilibrium—tendency to fall to the right and deviation of the right upper extremity—would be in favor of a diagnosis of involvement of the frontal lobe or of a disease in the deeper vestibular pathways.

CASE 2.—A man, aged 46, with an extensive deep cranial defect in the right temporal region, presented the following clinical picture: difficulty in lateral gaze to the left, a wider left palpebral fissure, diminution of sensibility in the skin and joints with astereognosis on the left, left hemiparesis with a crossed facial paresis on the right, slight ataxia and pastpointing of the left upper extremity, tonic dorsiflexion and supination of the left foot when the sole was stroked, a positive tonic neck reflex, passive synkinesiasis (in the same direction) in the left elbow joint and hand with athetoid movements in the fingers, tonic rigidity (in extension) of both lower extremities, more marked in the left, and epileptiform seizures, with tonic movements of the head and arm and postparoxysmal paraphasia. The patient was left-handed. Tonic athetoid movements of the fingers of the left hand were best elicited by stroking or pricking the skin of any part of the body and by sensory stimuli of light and sound. The movements also appeared during active and passive movements of the arms and during passive movements of the unaffected arm at the elbow and wrist with synkinesias, in the same direction, in the left upper extremity. In this case, too, summation of stimuli was necessary to elicit the athetoid movements of the fingers. The dyskinetic phenomena disappeared with the cessation of the stimuli. Although stimulation of any part of the body produced the abnormal motor phenomena, they were more spontaneous and more intense on stimulation of the palm of the right hand, especially on its radial aspect. On stimulation of the left lower extremity there appeared a gradually increasing extension at the knee and a dorsal flexion at the ankle joint.

In this case, hemiparesis with the evidences of limb-kinetic apraxia, hemihypesthesia, disturbances in the sense of position and astereognosis are attributed to extensive involvement of the right central convolutions and of the subcortical white matter. The various tonic phenomena, as well as the athetoid movements, are due to involvement of the mesencephalon, especially of the red nucleus. Involvement of the brain stem, especially of the substantia nigra, probably accounts for the passive synkinesias. The alternating facial hemiplegia and the disturbances of the extra-ocular movements are due to lesions in the region of the pons and the corresponding nuclei on the floor of the aqueduct. The pastpointing in the presence of evidences of loss of irritability of the right vestibular nerve (proved by caloric tests) can be accounted for only by a lesion of the deeper vestibular tracts or centers.

These localizations, though probably correct, have not been proved by necropsy. Jacoby reports the two cases because they confirm Alexander's investigations as to the significance of kinesthetic stimuli in the production of complicated synkinesias and also Kleist's theory of the significance of the substantia nigra as an intercalating station for the transformation of sensory stimuli into synkinetic phenomena.

KESCHNER, New York.

BASAL ANAESTHETICS AND ALLIED SUBSTANCES. H. W. FEATHERSTONE, Brit. M. J. **1**:322 (Feb. 24) 1934.

Noninhalational narcotics are solids which are administered to the patient in solution in water; in view of the incomplete nature of the anesthesia they produce when given in safe doses they have been termed "basal anesthetics." Sodium amytal,

pentobarbital sodium, secondary butyl beta bromallyl barbituric acid sodium salts, hexyl ethyl barbituric acid, sodium butyl ethyl barbiturate and the sodium salt of N-methyl-cyclo-hexenyl-methyl barbituric acid all belong in this large new group of barbiturates. The chemistry of the barbiturates is important but somewhat obscure. They are derivatives of urea.

For practical purposes the effects of these drugs can be divided into three stages: (1) hypnosis, in which the patient can be roused to speak and even to voice his disapproval if pinched but subsequently has little or no memory of the incident; (2) inebriation, in which he moves when the skin is stimulated and may be restless but shows no signs of consciousness, and (3) anesthesia, in which there is no response to painful stimuli but often respiratory depression, a decrease in the blood pressure and a tendency for the tongue to fall back in the mouth. Shock and pulmonary edema leading to bronchopneumonia may result from a particularly large dose of barbiturate.

The use of the basal anesthetics is indicated especially for the excitable, apprehensive vigorous person who frequently requires a large dose of anesthetic and careful handling. Patients with alcoholism are especially difficult to handle, and for them the barbiturates are often most helpful and comparatively safe. In some cases a small dose of opium alkaloids beforehand and darkening of the bedroom will prepare the patient for the rapid absorption of the barbiturate. For patients who require repeated minor operations, and particularly for children, pentobarbital sodium administered orally is a great boon. The dose should be small, 1 grain (0.065 Gm.) or less for a child of 4 years. It is frequently advisable to give the sedative at night so that he will fall asleep and general anesthesia can be administered in the morning without waking him. If the barbiturate is not effective or is vomited, a small dose of avertin may be given by rectum. These methods enable one to anesthetize small children repeatedly without their being aware that they have been operated on. The frequency of postanesthetic vomiting is reduced by employing any basal narcotic, but vomiting due to hepatic weakness, intestinal obstruction or other causes may be increased. For cerebral surgical measures, pentobarbital sodium orally with opium alkaloids, followed by a little anesthetic and some oxygen, has yielded good results. In gynecological plastic surgery, hemorrhage is thereby reduced. Featherstone is not enthusiastic about the barbiturates for use in surgical procedures on the thyroid; in dental surgery they should be used with discretion. He summarizes his experience with the barbiturates in obstetrics as follows: A full dose of sodium amytal or of pentobarbital sodium, injected intravenously just before full dilatation, will produce painless labor; there do not seem to be any contraindications to its use if it is given slowly, except the danger of precipitate delivery of the head. With avertin, however, labor tends to be delayed, and the child's respiration may be depressed. Delirium tremens, mania from various causes and persistent hiccup are examples of conditions which have benefited greatly from the use of basal narcotics. There is a risk of pneumonia in persons who have received a large dose of a barbiturate. Therefore, in the presence of inflammation of the lungs, empyema and even catarrhal conditions of the bronchi and upper air passages, barbiturates should be withheld. This is not applicable to avertin. Toxic conditions of the liver or kidneys, or toxic conditions generally which might affect these organs, are contraindications for the use of barbiturates or avertin. In cases of coma produced by barbiturates, the drug can be detected in the cerebrospinal fluid; removal of a quantity of the fluid by lumbar or cisternal puncture produces at least a temporary improvement. In the presence of heart disease, if signs of active toxemia are absent, the use of avertin with gas and plenty of oxygen is valuable.

Featherstone's conclusions are as follows: It does not seem wise to give a basal narcotic unless the patient has been examined carefully beforehand. Administration of the barbiturates by the oral route is convenient, but it may be ineffective, or, on the other hand, the effect may be too pronounced. The intravenous route is not always safe. Avertin seems to be less convenient to administer but it is perhaps more reliable; the dose can be assessed with greater accuracy, and the liver appears to be able to detoxicate the simple molecule of avertin rapidly.

FERGUSON, Niagara Falls, N.Y.

MENTAL DISEASE SITUATIONS IN CERTAIN CULTURES—A NEW FIELD FOR RESEARCH. JOHN M. COOPER, J. Abnorm. & Social Psychol. **29**:10 (April-June) 1934.

The study of mental diseases among primitive people is an almost virgin field for social and psychiatric research. There is at present detailed information for four or five primitive areas or cultures and only scattered references on the remaining areas. A great many, probably the great bulk, of the psychopathic phenomena observed among primitive people are duplicated in modern civilization. There are, however, certain characteristic mental disorders among primitive peoples, types that occur with striking emphasis and frequency and that are more or less peculiar to a particular primitive group. The Eastern Cree Wihtiko psychosis and the Malayan "amok" aberrations are types of mental disorder that are in the main confined to these two peoples respectively.

The Wihtiko psychosis is characterized by a psychopathic craving for human flesh and by a delusion of transformation into a Wihtiko, a supernatural being feared by the Eastern Cree. The origin of this seems to be the fact that cannibalism was resorted to by the Eastern Cree when starvation threatened. The solution of the conflict between hunger and the rigid tribal taboo against cannibalism has resulted in this distinct mental aberration. It seems significant that among the Eastern Crees the forms of mental disorder are almost exclusively, apart from the rare Wihtiko psychosis, of an introvert order. Actually the Eastern Cree culture may be said to have an introvert trend. Fighting, wounding and bodily violence and murder are frowned on by their culture and are almost unknown. It seems reasonable, then, that the relationship between the introvert individual Cree psychopathic phenomenon and these introvert Cree cultural phenomena is not a casual one. A surprisingly high incidence of echolalia and echopraxia is found among Eastern Crees—evidence of the schizoid reaction phenomenon. Hysteria is also common in the form of convulsions, catalepsy, anesthesia, hallucinations and melancholia.

Among the Malays two forms of mental disorder are detailed. These are latah and amok. Certainly in many cases of running amok there is little or no mental derangement. In some of the few cases in which the one who has run amok has survived the weapons of the neighbors he has claimed that his vision was darkened during the attack, but this is not an uncommon excuse given by a Malay who has neglected his duty and wishes to offer an alibi. Among the Yahgan and Ona, Fuegian tribes of South America, who are living on the same low level of material culture as are the Crees, hysterical outbreaks are not infrequent. After a period of brooding the victim may dash wildly out of the tent, running until exhausted, and at such times may injure or kill. Two cases of anesthesia during hysterical crises of women are reported.

Hysteria is common among the Greenland Eskimos. Of twenty Eskimo women on the *Roosevelt*, eight were subject to attacks. The most common symptoms consist of stripping off all the clothes, even in severe subzero weather, and dashing off over the ice. Hirsch's survey of the medical literature prior to 1881 seems to show that hysteria is extremely common, too, in many other regions and among many other peoples—parts of Central Siberia, certain of the Polynesian Islands, the territory of the Hottentots, Abyssinia, parts of North Africa and various areas in Central and South America.

WISE, Howard, R. I.

A THOUSAND CASES OF ATTEMPTED SUICIDE. FREDERICK C. LENDRUM, Am. J. Psychiat. **13**:479 (Nov.) 1933.

This article presents an analysis of a thousand genuine attempts at suicide made in Detroit between the fall of 1927 and the spring of 1930. Only cases brought to the attention of the police or other city officials were included. To some extent the series is a selected one, for wealthy patients were often not brought to the Receiving Hospital, and persons who used rapidly fatal methods did not reach the hospital alive.

Women made attempts more frequently than did men, but were successful less frequently. This is due, in part at least, to the preference of men for mechanical methods (shooting, hanging, etc.) which are likely to be more effective than poison (used by five sixths of the women). The median age was 33 for men and 24 for women. Of the men, 19 per cent were 45 or older; of the women, only 4 per cent fell into this group. Negroes made a disproportionately large number of attempts and were relatively less successful than white persons. Divorced women were involved with five times the expected frequency according to their general distribution in Detroit; otherwise marital status seemed to be of little significance in comparing the incidence of suicide with the norms. Protestants contributed twice their share to the suicide group; Jews and Catholics, much less than their share. The assigned motives were generally economic for men and emotional for women.

Unemployment appears to be a predisposing factor of importance. The incidence of unemployment in Detroit was 6.4 per cent, while 14.5 per cent of the suicidal group were unemployed. Lendrum compared the annual suicide rate with the stock market averages and found no correlation. Apparently unemployment during a depresson is less likely to lead to a suicidal attempt than isolated individual unemployment during a boom. The hour of admission to the hospital, which was usually the hour during which the attempt was made, was also studied. The low point was at 4 a. m. and the high point at 12 midnight. A steady rise through the day suggests the influence of fatigue. A special rise was noted between 6 and 7 p. m., possibly owing to the fact that this is usually an unoccupied hour devoted to conviviality. Fewer suicides were attempted on Friday than on any other day of the week, while Sunday had the largest number.

DAVIDSON, Newark, N. J.

CHANGES IN THE BRAIN IN CASES OF EXPERIMENTAL HYDROCYANIC ACID POISONING. A. MEYER, Ztschr. f. d. ges. Neurol. u. Psychiat. **143**:333 (Jan.) 1933.

There are few good studies on acute cyanic acid poisoning, because death is so rapid as to produce few changes in the nervous system. A few late cases are recorded. Schmorl reported the case of a patient who died after thirty-six hours. The brain showed symmetrical reddish-gray softenings in the pallidum. Edelmann reported a case in which the patient died after twenty-three hours; there were marked hyperemia, fresh symmetrical softenings in the corpus striatum and involvement of the inner part of the lenticular nucleus.

Meyer reports on seven dogs which were poisoned with a 10 per cent solution of potassium cyanide and died from two to five days later. In dog 1, which died after four days, there were hyperemia of the brain, bilateral softenings in the substantia nigra, a subpial hemorrhage in the cerebellum and severe changes in the Purkinje elements. In dog 2, which died in five days, there were typical ischemic disease of the ganglion cells everywhere in the cortex, swelling of the endothelium, ischemic changes in the pallidum, caudate and thalamus, changes in the cornu Ammonis and severe changes in the Purkinje cells. In dog 3, which died after five days, there were bilateral softening in the pallidum, with the inner segments more affected, softening in the callosum, endothelial swelling and perivascular proliferation of lymphocytes in the cortex, swelling of all the glial elements, with development of gitter cells, and focal loss of ganglion cells in the cortex. In a rabbit killed after one week, there was proliferation of vessels and protoplasmic astrocytes in many parts of the cortex. The ganglion cells were degenerated, and there were focal areas of loss of cells. Microglia cells were proliferated and converted into gitter cells. Other animals showed ischemic changes in the cells in the putamen and gliosis in the corpus callosum.

The changes found were chiefly of a vascular character: ischemic cell changes in the early stages and softenings later. Meyer found just as pronounced endarteritic changes in these animals as in those with carbon monoxide poisoning. Similarly the softenings in the pallidum were like those seen in the animals with

carbon monoxide poisoning; so, too, was the softening in the substantia nigra. The changes in the cornu Ammonis are the first of the kind that have been reported in animals.

ALPERS, Philadelphia.

TREATMENT AND CONTROL OF ESSENTIAL HYPERTENSION. H. O. GUNEWARDENE, Brit. M. J. **2**:1114 (Dec. 16) 1933.

This investigation and the measures outlined for treatment in cases of essential hypertension were stimulated by the report of Cyriax in 1917 that high blood pressure was relieved by "mobilization of the spinal column," by which was meant active and passive movements of the vertebral joints and passive manipulations, vibrations, pétrissage, etc., of the erector spinae muscles. Gunewardene modified the method by substituting electrical stimulation of the skeletal muscles and subjecting patients with high grades of hypertension to treatment along these lines. As a preliminary, each patient was tested to see what effect the resulting muscular contractions had on the pulse rate, since some were on the verge of cardiac failure. In none of the patients did the pulse rate rise; in most it dropped considerably.

The machine used generated a faradic current, with a Lewis Jones interrupter in circuit to prevent irregular contractions and uneven, unpleasant shock. The writer thinks that in the absence of electricity, massage will answer. When the diastolic blood pressure drops below 110 as a result of treatment the patient is taught exercises with which the muscles may be kept in action, particularly the muscles of the trunk, or advice is given that mild exercise may be resorted to. The warning is given that the patient should be carefully watched, particularly when cardiac enlargement and symptoms are present, or the physician may some day be called on to face a charge of electrocution when death due to heart failure is attributed to electrical shock. Drugs may be resorted to to maintain the good results obtained. The results from this treatment indicate that in some cases of hyperplasia the blood pressure drops to a low limit, even to a normal level, without rest or medicinal aid. In other cases the patient is relieved of his symptoms and proclaims that he feels better, but the pressure will not fall. Such a patient shows impaired renal function as gaged by the urea concentration test. The heart enlarged as a result of the strain of hypertension becomes astonishingly smaller with the fall of pressure.

The writer is unable to give an explanation of the mechanism by which the reduction of pressure is brought about. He was encouraged to try it in the belief that sedentary occupation or lack of sufficient exercise plays an important part in the etiology of essential hypertension.

FERGUSON, Niagara Falls, N. Y.

SYRINGOMYELIA IN TWO SISTERS, ONE OF THEM WITH A CEREBELLAR CYST. L. VAN BOGAERT, Ztschr. f. d. ges. Neurol. u. Psychiat. **149**:661 (March) 1934.

There are about twenty reports of cases of familial syringomyelia, many of which are atypical. Van Bogaert records the occurrence of the disease in three members of a family previously reported on by Verboogen and van der Vielde. The family history was bad. The materal grandfather suffered from mental disease for many years. The mother was an alcoholic addict and had cerebral arteriosclerosis. The father was an alcoholic addict and died of delirium tremens. There were eleven children; four were healthy; four died of convulsions, typhus and tuberculosis, and three had syringomyelia. In one child this condition appeared at 8 years and in the other two at 12. Histologic study was carried out in one of the cases of syringomyelia and typical cavities were found in the spinal cord.

The problem is whether syringomyelia occurring in families differs in any way from the sporadic disease. To answer this, van Bogaert reports two cases of his own. The patients were descended from a father who died of myocarditis and a mother who died of bronchopneumonia. There were two healthy children. In one of the cases there were signs of a cerebellar cyst. Autopsy revealed a cyst of the left lobus semilunaris, a cleft in the left side of the medulla and syringomyelic cavities in the cord. Histologic studies showed gliomatosis in the lumbar region

and also in the cervical region of the cord. In the medulla there was a small slit, and in the cerebellum a cyst with smooth walls and without tumor; the cyst was surrounded by numerous sclerotic vessels. There was no ependymal epithelium anywhere in the cyst. There was no evidence anywhere of tumor formation. In the second case autopsy showed typical syringomyelic cavities in the spinal cord, most pronounced in the cervical region.

Van Bogaert asks whether these cases differ in any way from sporadic cases of syringomyelia; he concludes that they do not, either in the clinical or in the pathologic picture. The cerebellar cyst must be considered as being derived by cystic degeneration from a previous gliosis. The author suggests that some simple cerebellar cysts may be of syringomyelic origin. ALPERS, Philadelphia.

MYASTHENIA GRAVIS: THE EFFECT OF TREATMENT WITH GLYCINE AND EPHEDRINE. WALTER M. BOOTHBY, Arch. Int. Med. **53**:39 (Jan.) 1934.

The weakness accompanying myasthenia gravis is presumably due to a disturbance of the intermediate chemical reactions concerned with muscular contraction or relaxation. Glycine is one of the constituents of muscle protein. It is administered in myasthenia gravis in a daily dosage of 30 Gm. The cases of twelve patients treated at the Mayo Clinic are here reported; all presented typical myasthenia gravis. The therapeutic regimen included ephedrine, 3/8 grain (0.024 Gm.), twice daily, in addition to the glycine. The twelve patients are divided into four groups according to severity. Group 1 consisted of four mildly affected patients, all of whom could walk freely. The chief weakness was exhibited in the muscles of deglutition. All improved after from eight to twelve months of glycine-ephedrine treatment and were able to carry on their lives in a reasonably comfortable manner. Group 2 consisted of five patients able to walk only a short distance alone; all improved, although the degree of improvement varied; three were able to maintain their improvement on a decreased dose. Only one patient was placed in group 3. She improved on ephedrine alone, which was taken for eighteen months. This regimen transformed her from a bedridden invalid into a fairly active woman. For six months she has supplemented the ephedrine with glycine, but no alteration in the rate of improvement has been noted. The two patients in group 4 were in the advanced stage of the disease and showed little improvement.

Reviewing the whole series, Boothby points out that ten of the twelve patients showed definite improvement on the glycine-ephedrine regimen. He believes that this combined medication is indicated in cases of myasthenia gravis.

DAVIDSON, Newark, N. J.

CRANIAL NERVE PALSIES AS A MANIFESTATION OF PERIPHERAL NEURITIS IN ALCOHOLIC INSANITY. D. J. O'CONNELL, J. MCLEMAN AND RUBY STERN, J. Ment. Sc. **80**:103, 1934.

Palsy of the cranial nerves in cases of alcoholic peripheral neuritis is rarely mentioned in neurologic literature. Three cases are cited by the authors, all of which occurred in physicians admitted to St. Andrews Hospital because of excessive use of alcohol. In the first case the patient showed complete bilateral palsy of the external rectus muscle with signs of peripheral neuritis in the legs. In the second case there were also complete bilateral palsy of the sixth nerve affecting the external rectus muscle, partial bilateral palsy of the third nerve and slight drooping of the mouth on the left, in addition to peripheral neuritis in the arms and legs. The third case was a typical instance of delirium tremens; the patient gave an account of a previous diplopia, which is interpreted by the authors to mean that he had had a transient ocular palsy. The interesting point about these cases is that while the peripheral neuritis in the extremities persisted for a long time, the ocular palsies disappeared within a fortnight. This is explained by the fact

that neuritis in the legs is probably of long standing, whereas cranial neuritis is due to acute alcoholic poisoning of the cortical nerve cells. Recovery from the ocular palsy is usually ushered in by a gross horizontal nystagmus, which is probably due to ataxia in connection with weakness of the respective muscles. The blood cholesterol was unusually low in all three cases, and the authors agree with Leary's theory (*New England M. J.* **205**:231, 1931), that since alcohol is a solvent of cholesterol it is difficult for cholesterol to precipitate into a body permeated by alcohol.

KASANIN, Howard, R. I.

MENTAL HYGIENE VERSUS PSYCHOANALYSIS. MILTON HARRINGTON, Psychiatric Quart. **7**:357 (July) 1933.

It is the fashion for freudians to condemn present methods of mental hygiene as superficial and inadequate. Their hypothesis rests on the assumption that mental abnormalities are the fruit of childhood traumatisms and subconscious sexual perversions. On this basis, advice to avoid worry and anger, to obtain rest and relaxation, to cultivate a sense of humor, to face life squarely and to seek favorable environments is futile, for this advice does not touch the subconcious forces which breed mental disorder. From this point of view mental hygiene today is improperly named; it is only social psychiatry.

Harrington, however, rejects this attitude. He believes that behavior cannot be adequately expressed in terms of motive or desire, but that it is the response to environmental stimuli of the complicated mechanism of the body-personality unit. When this mechanism displays a fault, it is because the machine itself is defective or the forces which met it have been too severe. Mental ills can be due only to bad heredity, faulty environment, somatic injury, disease, improper education or some combination of these. This points the way to proper mental hygiene, breeding healthier and more efficient persons, providing education which will enable human beings to make the most of their personalities, preserving bodily health and supplying an environment favorable for wholesome self-expression. This, he believes, is more likely to succeed than the analytic technic, which he condemns as "muck-raking for pervert sexual desires in the cesspool of the unconscious."

DAVIDSON, Newark, N. J.

TUBERCULOMAS OF THE LENTICULAR NUCLEUS: A CLINICAL AND ANATOMIC CONTRIBUTION. G. PINTUS, Arch. gen. di neurol., psichiat. e psicoanal. **14**:279, 1933.

Pintus reports the case of a woman, aged 32, who, during the seventh month of pregnancy, began to have headaches. A few months later, "pins and needles" paresthesia appeared on the left side of the body, at first in the foot, then in the thigh, then in the left hand and arm and then in the left side of the face. Vision gradually failed, and about eight months after the onset of the headache complete left-sided hemiplegia with contracture developed. A diagnosis of a tumor of the brain was made. The patient died following an operation. Autopsy revealed a solitary tuberculoma, 3.5 cm. in diameter, in the right lenticular nucleus compressing the thalamus and destroying the internal capsule. Pintus points out the extreme difficulty of making a localizing diagnosis of a tumor of the striatum during life. He believes that one should assume a striatal localization of a tumor when, along with the general signs of intracranial neoplasm, the symptoms of sensory and motor deficit develop with great delay after the onset of the general symptoms of the neoplasm and when all other localizations are excluded. On the grounds of clinical symptomatology it is impossible to differentiate between tumors of the lenticular nucleus and those of the caudatum. Pintus concludes his report with a discussion of the histopathology of tuberculoma of the brain with reference to the solitary tuberculoma and multiple agglomerated tuberculomas.

YAKOVLEV, Palmer, Mass.

THE PRODUCTION OF CARDIAC IRREGULARITIES BY EXCITATION OF THE HYPOTHALAMIC CENTERS. B. B. DIKSHIT, J. Physiol. **81**:382 (June 9) 1934.

Brow, Long and Beattie (1930) showed that decerebration of cats at the Sherrington level abolished the extrasystoles that were induced by light chloroform anesthesia. They concluded that there is some mechanism above the Sherrington level which controls the cardiac arrhythmias. They apparently concluded that certain centers in the hypothalamus control the rhythm of the heart.

Dikshit (1934) showed that injection of acetylcholine into the lateral ventricles of cats caused irregularities in a heart which had been perfectly regular. These experiments suggest that the irregularities are produced by the action of the drug on certain nerve centers in the midbrain. "The experiments of Brow, Long and Beattie have proved the existence of a center in the hypothalamus, stimulation of which can cause cardiac extrasystoles. Experiments described in this paper support that view. The fact that all experimental procedures which produced irregularities were effective after bilateral vagal section and atropinization of the animal proves that the efferent impulses which provoke cardiac irregularities do not pass through the vagus but probably through the sympathetic."

The irregularities were produced by stimulation of the central vagus nerve and by the injection of small quantities of acetylcholine into the cerebral ventricles. Similar irregularities can be produced by intraventricular injections of caffeine and nicotine or by clamping both carotid arteries. ALPERS, Philadelphia.

CLASSIFICATION OF PRISONERS. JAMES L. MCCARTNEY, Psychiatric Quart. **7**:369 (July) 1933.

McCartney describes the classification clinic at the Elmira Reformatory, an institution which receives over a thousand new prisoners annually. Of these, 35 per cent are classified as "neuropathic," 8 per cent as psychotic or potentially so, 24 per cent as feebleminded and 33 per cent as normal. Each newly admitted prisoner is placed in the reception building for four weeks. During this time thorough social and medical histories are obtained and verified by correspondence with friends, employers and relatives. Physical, neurologic and laboratory examinations are made, and psychologic tests are given. At the end of this period the case is considered in the classification conference. This body consists of the psychiatrists and psychologists, social workers, physicians, disciplinarian, chaplains, vocational director, and educational director and other interested officers of the institution. The dossier of each case is presented and discussed, and the prisoner is interviewed at the conference. If further psychiatric observation seems necessary the inmate is transferred to a special unit where these studies can be made. Otherwise, recommendations for scholastic and vocational placement are forwarded by the examining body. It is McCartney's opinion that with the classification system properly carried out, two thirds of the inmates could be housed in minimum security dormitories instead of locked cells, at a great saving to the state and with much benefit to the prisoner. DAVIDSON, Newark, N. J.

PAPILLARY STASIS IN ENCEPHALITIS. I. ALFANDARY and S. STAYITCH, Rev. d'oto-neuro-opht. **12**:503 (July-Aug.) 1934.

Papillary stasis may at times accompany encephalitis of any origin, although in such a case it is most often inflammatory papillitis rather than choked disk of mechanical origin. The important differentiation between tumor and encephalitis is sometimes difficult.

A child, aged 10 years, who was admitted to the hospital on Oct. 19, 1933, for two weeks before had had general malaise and latterly vomiting four or five times daily. Suddenly violent headaches occurred and persisted and were followed by epileptic convulsions, fever, a high leukocyte count (from 25,000 to 32,000), amaurosis, a positive Babinski sign and bilateral papillary stasis. The pupils were dilated, but the light reflex persisted. One attack of epilepsy was of the jacksonian

type. After a few days the child was taken home, and within a few days the alarming symptoms disappeared. Reexamination ten weeks later showed all in order except a slight temporal pallor of the disks. Infectious meningitis and cerebral tumor could be eliminated. Abscess of the brain appeared probable at one period, and even later the possibility of a latent abscess was entertained. Acute panencephalitis of the Strümpel-Leichtenstern type is the probable diagnosis. Papillary stasis does not always mean increase of intracranial pressure, and still less may one deduce from it indication for surgical intervention.

DENNIS, San Diego, Calif.

MELANCHOLIA: A CLINICAL SURVEY OF DEPRESSIVE STATES, AUBREY J. LEWIS, J. Ment. Sc. **80**:277, 1934.

In a comprehensive and scholarly paper of over one hundred pages, Lewis does a great service to psychiatry by analyzing the symptomatic and clinical picture in sixty-one of his own cases of depression. The various aspects of the clinical pictures are reviewed in the light of current knowledge about such symptoms and the differences between current knowledge and opinions in Anglo-American and those in Continental psychiatry. Lewis stresses the frequency of obsessive states in manic-depressive psychoses and is critical about usual notions in reference to delusions and the patient's attitude to his environment. In reference to psychomotor retardation, he points out that inhibition would be a more accurate term and that difficulty in thinking lies largely in the field of organized thought directed toward some definite goal, such as solving a psychologic problem or a puzzle. Ordinary undirected associations run with remarkable rapidity and fluency. Anxiety is, even in its limited sense as used in the English language, frequent and severe in cases of manic-depressive psychosis. The fact that Lewis waited for three years after his paper was written to make sure that all his cases were true cases of affective disorder testifies to his thoroughness and intellectual honesty. The paper is far too comprehensive for an ordinary review.

KASANIN, Howard, R. I.

CHRONIC SUBDURAL HEMATOMA. J. J. KEEGAN, Arch. Surg. **27**:629 (Oct.) 1933.

Five cases of chronic subdural hematoma are reported, and the etiology and treatment of this disease are discussed. Mild trauma to the head results in tearing the small veins which course from the brain to the superior longitudinal sinus. In severe injuries to the head the resulting marked cerebral edema mechanically compresses torn veins, favors clotting and prevents large subdural collections of blood. In milder forms of injury the absence of appreciable reactive edema and the continuance of normal activity and straining favor bleeding from the rigid walls of the opening in the superior longitudinal sinus.

In patients with cerebral atrophy the cerebral hemispheres appear suspended from the superior longitudinal sinus by their venous connections and render these subjects more susceptible to subdural hemorrhage.

The more conservative and recently advised management of exploration and drainage by trephination was employed, without removal of the hematoma sac, permitting the gradual restoration of the intracranial pressure and structural relations, except in cases in which specific indications (continued bleeding) rendered more radical surgical procedures imperative.

SPERLING, Philadelphia.

DISTURBANCES OF EQUILIBRIUM AND OF MOTOR COORDINATION IN LESIONS OF THE PREFRONTAL LOBE. GIOVANNI DE NIGRIS, Arch. gen. di neurol., psichiat. e psicoanal. **14**:302, 1933.

After a brief review of the symptomatology in cases of lesions of the prefrontal lobe reported in the recent literature, de Nigris reports the study of four personal cases with surgical or postmortem verification of such lesions (tumor in three cases and cerebral softening in one). Disturbances of equilibrium are prevalent

in cases of lesions of the frontal lobe. The symptoms are usually unilateral and contralateral to the seat of the lesion. In cases of tumor of the frontal lobe it is seldom possible to recognize solely on the ground of the clinical character of the ataxia whether it is due to a frontal or to a cerebellar disease. The discrimination is, however, possible when one takes into account the so-called neighborhood symptoms (atrophy of the optic nerve, anosmia and facial paralysis of the central type) which must therefore always be carefully observed. In cases of unilateral lesion of the frontal lobe, bilateral symptoms of the cerebellar type may occur. In such cases it is necessary to admit the possibility of direct interference with cerebellar functions either by compression of this organ or by the effect of contrecoup.

YAKOVLEV, Palmer, Mass.

A BRIEF REVIEW OF FEVER THERAPY IN NEUROSYPHILIS. HARRY BECKMAN, Arch. Dermat. & Syph. **28**:309 (Sept.) 1933.

The induction of tertian malaria, although the most popular, is not the only good method of inducing fever in the treatment of neurosyphilis. Patients who do not respond favorably to infection with the tertian parasite may often be treated successfully by inoculation with the quartan or subtertian (malignant) plasmodium. This form of treatment should not be restricted to dementia paralytica, as good results have been reported in the treatment of diffuse neurosyphilis and of tabes dorsalis. Rat-bite and relapsing fevers are less effective, harder to transmit and more likely to be associated with untoward results. For extra-institutional treatment, Beckman recommends typhoid-paratyphoid vaccine. Although not as effective as malaria, it is safer and more convenient. Another convenient method of inducing fever is to inject intramuscularly 1 or 2 cc. of a 1 or 2 per cent solution of sublimed sulphur in olive oil. This is given in increasing doses, every four or five days, for ten injections. Diathermy and hot baths are effective but of limited use because of the necessity of cooperating with trained physical therapeutists. A patient's chance of recovery following malaria therapy, Beckman estimates, is from 20 to 30 per cent.

DAVIDSON, Newark, N. J.

SOME OBSERVATIONS ON LIPOID METABOLISM IN MENTAL DISORDERS. J. S. SHARPE, J. Ment. Sc. **80**:75, 1934.

In this paper Sharpe does not state how many cases were studied, and his conclusions are somewhat vague, without any indications that control material was used. He concludes that the lecithin content of the blood in cases of mental disease shows no important variation from the normal. In early phases of schizophrenia the cholesterol content is decreased by about 25 per cent and ranges around 0.19 per cent. However, in chronic cases the cholesterol rises above normal to 0.34 per cent. The hyperactivity of the suprarenal glands is given as a reason (?). A high blood cholesterol is seen in persons with recurrent manic attacks, particularly during acute attacks. The coefficient of utilization is also high, suggesting an increased metabolic rate. Sharpe postulates the presence of a powerful depressor substance in certain melancholic and confusional states; this substance has a choline-like action on the isolated heart of the frog and is antagonized by epinephrine. The article is written so vaguely that it is difficult to understand the basis on which the author makes his conclusions.

KASANIN, Howard, R. I.

THE LOCALIZATION OF THE PATHS SUBSERVING MICTURITION IN THE SPINAL CORD OF THE CAT. F. J. F. BARRINGTON, Brain **56**:126 (July) 1933.

Lesions were made in different parts of the spinal cord of cats; the cats were kept alive, and the presence or absence of any defect of micturition was noted. The two principal defects were the presence of residual urine and the loss of consciousness of the need to micturate. In the anterior lumbar region (last

thoracic and first two lumbar segments), both the centrifugal and the centripetal path are situated in the part of the dorsal half of the lateral column extending inward for a third of its thickness. Twelve experiments in the posterior lumbar region gave consistent results, the paths of micturition being in the same position as in the anterior lumbar region. There is an extensive but incomplete crossing of the centrifugal and the centripetal path between the anterior lumbar region and the origin of the pelvic nerves. In the cervical and thoracic regions, both paths are in some part of the dorsal half of the lateral column or in the wedge-shaped area of gray matter subtended by this toward the central canal.

MICHAELS, Boston.

THE DEPRESSION STEW. LOUIS A. SCHWARTZ, J. Crim. Law & Criminol. **24**:1067, 1934.

In an address to the Detroit Chapter of the American Association of Social Workers Schwartz asserts that the present economic depression is the consequence not of one but of a multiplicity of etiologic factors, most of which are economic; treatment, therefore, must necessarily lie in the economic sphere. Some thought is given to the relationship of the individual to the world about him and to the projection of the individual's personal failures. The question is raised whether or not the rise of civilization is now being followed by a decline and decadence. Some discussion is also devoted to such social phases of the problem as the prolongation of dependency due to modern educational methods, probation and communal activities; the last phase is discussed from the point of view of what has been accomplished thereby in Germany. The change in modern family life due to the economic upset which has, to some degree, reversed the relationships of fathers and mothers to their children is also adverted to briefly. SELLING, Chicago.

THERAPEUTIC MALARIALIZATION OF GENERAL PARALYTICS IN THE TROPICS. A. W. H. SMITH, J. Ment. Sc. **79**:94, 1933.

Smith studied the problem of the treatment of patients with dementia paralytica with malaria in the Central Mental Hospital of the Federated Malay States, where malaria is endemic. The diagnosis was established by positive findings in the blood and spinal fluid. Of the fifty-six patients inoculated, forty-two failed to contract malaria. Of the fourteen patients who contracted malaria, only four were improved, six were not improved, and two died. Smith believes that artificial malarialization fails in the tropics because of the large previous infection of the patients. He believes that dementia paralytica is as frequent in the tropics as in temperate climates; he admits, however, that tabes is extraordinarily rare in Asia. The reason for the relative infrequency of involvement of the central nervous system by the spirochete is explained on the theory that the metabolism of the oriental races tends to develop dermotropic rather than neurotropic lesions.

KASANIN, Howard, R. I.

THE EFFICACY OF PRISON MENTAL TESTS AS A GUIDE TO REHABILITATION. WALTER WEBSTER ARGOW, J. Crim. Law & Criminol. **24**:1074, 1934.

Prisons may cease to be institutions of unprofitable punishment and become shops of human salvage where unknowns can be analyzed qualitatively and quantitatively if proper mental tests are made and adequate attention is given to the treatment indicated by the results thus obtained. No test can be expected to function effectively, however, unless there is established some rapport between the examiner and the patient. At present the entire system of penology is based on the old vendetta system—hurt and hurt back. Forceful measures will be required to abolish this (and it must be abolished) if the science of criminology is ever to aid either the criminal or society. The present task is to get trained workers into the jails and assure them freedom of operation. Argow, however, cannot but

view pessimistically the question of how long it will take the public and the old-school administrators to learn that this is the only way to curtail the nation's crime bill.

SELLING, Chicago.

THE BASAL METABOLISM IN PERNICIOUS ANEMIA AND SUBACUTE COMBINED DEGENERATION OF THE SPINAL CORD. M. M. SUZMAN, Am. J. M. Sc. **184**:682 (Nov.) 1932.

A definite difference, statistically significant, was found to exist in the basal metabolic rate in sixty-five cases of pernicious anemia without involvement of the spinal cord and sixty-five cases of pernicious anemia with involvement of the spinal cord. In the former group, 41.5 per cent showed a basal metabolic rate above 10 per cent; in the latter, 43.1 per cent showed a basal metabolic rate of 10 per cent or less. The difference between the two groups is more than can be accounted for by differences in the red blood cell levels. Although neuromuscular disability is not incompatible as a factor to account for the differences of the basal metabolic rate, the evidence is not conclusive.

MICHAELS, Boston.

AN OPHTHALMOSCOPIC SIGN AND DISTURBANCE OF THE RETINAL ARTERIAL PRESSURE IN PATIENTS SUFFERING FROM CEREBRAL CONCUSSIONS. C. TIRELLI, Ann. d'ocul. **170**:703 (Aug.) 1933.

Tirelli observed thirty-four cases presenting syndromes of concussion without concomitant lesions of the cranium. He points out that: 1. Changes in the fundus occur frequently in the simple syndrome of concussion without the presence of lesions in the bony skeleton. Among these, the most common is the peripapillary stria, similar in form to that described by di Marzio in serous meningitis and called "peripapillary retinal edema." 2. The relation between the retinal diastolic pressure and the brachial diastolic pressure is closer than normal in a large percentage of cases. 3. The pressure of the cerebrospinal fluid shows a direct relation to the retinal arterial pressure.

BERENS, New York.

SOCIAL REACTION OF RIGHT AND WRONG. TRIGANT BURROW, J. Crim. Law & Criminol. **24**:685 (Nov.-Dec.) 1933.

Every man (including the neurotic person and the criminal) at all times does what is "right." As the neurotic and criminal types are the most "obstinately right," economic insecurity and ethical instability have become the two major phenomena in the turmoil of today. The condition is social. Society must face it. If the sense of what is called "criminal" may be traced to the sense of what is called "right," if the sense of right and wrong governing normal behavior may be identified with the sense of right and wrong governing the insane and the criminal and if it can be shown that where one's advantage lies there lies one's sense of right and wrong, present systems for controlling human conduct will give way to saner, more scientific methods.

SELLING, Joliet, Ill.

SYRINGOMYELIC COMPLICATIONS OF SPINA BIFIDA. FRANK A. TURNBULL, Brain **56**:304 (Sept.) 1933.

A case of cervical spina bifida is reported in which there developed in early adult life signs suggesting a syringomyelic lesion of the spinal cord. At 1 year of age, a pedunculated tumor was removed from the back of the neck, disclosing the stalk of a meningocele. The patient was completely incapacitated by an advancing lesion of the spinal cord and died following laminectomy at the age of 32. Partial failure in closure of the embryonic medullary groove initiated the disease, which resulted in the formation of multiple syringomyelic cavities. There was a progressive disturbance in the blood supply of part of the cervical portion of the cord, and a small amount of neoplastic tissue was observed at the site of greatest disturbance of the cord.

MICHAELS, Boston.

EVIDENCE OF AN ACETYLCHOLINE-LIKE SUBSTANCE IN THE BLOOD OF THE LINGUAL VEIN AFTER STIMULATION OF THE LINGUAL NERVE. W. FELDBERG, Arch. f. d. ges. Physiol. **232**:88, 1933.

Dale had assumed that the vasodilatation and the contracture observed in the degenerated muscles of the tongue after stimulation of the lingual nerve are due to the production of acetylcholine or a similar substance. It was, however, not possible to prove this theory at that time, as the blood quickly destroys acetylcholine. The author uses the experience of Loewi and Navratil and others that physostigmine inhibits the destruction of acetylcholine. After intravenous injection of physostigmine in dogs he found that stimulation of the lingual nerve was followed by the appearance of an acetylcholine-like substance in the lingual vein. This corroborates the theory of Dale.

SPIEGEL, Philadelphia.

LEUKEMIC RETINITIS: MODIFICATIONS OF THE OPHTHALMOSCOPIC APPEARANCE IN RELATION TO THE PHASES OF CLINICAL EVOLUTION. P. BONNET and PAUFIQUE, Ann. d'ocul. **170**:885 (Oct.) 1933.

Typical leukemic retinitis, essentially characterized by edema of the retina, venous dilatation and exudates, hemorrhages and leukocytic infiltrations, is a manifestation of the onset of myeloid leukemia. It does not reappear during the disease, even if an acute attack occurs which clinically resembles the onset. Leukocytic infiltration of the sheaths of the blood vessels appears to be the most constant sign of leukemic retinitis. In serious forms of leukemic retinitis the importance of the participation of the choroid is evident ophthalmoscopically. Areas of atrophy of the pigmented epithelium remain as evidence of previous underlying disease of the choroid.

BERENS, New York.

INVOLVEMENT OF THE EIGHTH NERVE IN SYPHILIS, WITH SPECIAL REFERENCE TO THE RESULTS OF TREATMENT. ANTONIO CIOCCO and ALBERT WEINSTEIN, Am. J. M. Sc. **187**:100 (Jan.) 1934.

The hearing of 286 persons with a well established diagnosis of syphilis was examined with an audiometer, supplemented in most cases by Weber's, Schwabach's and Rinne's tests. Shortened bone conduction in the presence of good hearing has not been observed except in cases of loss of the high tones. A diagnosis of neurosyphilis based only on impaired function of the eighth nerve in a patient with syphilis is not justified. It is concluded that antisyphilitic treatment has no effect on hearing, either beneficial or detrimental, except in deafness associated with early meningeal neurosyphilis.

MICHAELS, Boston.

SPASTIC PARAPLEGIA IN ACHONDROPLASIA. E. FREUND, Arch. Surg. **27**:859 (Nov.) 1933

A case of spastic paraplegia is reported in a typical chondrodystrophic female dwarf, aged 21, with marked angular kyphosis at the second lumbar vertebra. The patient's condition became somewhat worse after laminectomy. Six cases of achondroplasia with neural symptoms in the lower extremities reported in the literature are reviewed. Deformity of the spinal column in achondroplasia is frequent, such as the presence of severe dorsolumbar kyphosis, with secondary marked arthritic changes resulting from the abnormal mechanical conditions of the spine. These abnormalities and narrowing of the spinal canal are believed to give rise to the neural symptoms by pressure on the spinal cord.

SPERLING, Philadelphia.

A CASE OF BRISSAUD'S HEMICRANIOSIS. G. B. SALVATOR, Ann. d'ocul. **170**:707 (Aug.) 1933.

Salvator reports a case of Brissaud's hemicraniosis in which symptoms existed for more than twenty years. In the early stages the symptoms were mild, but

in the last few years, especially in the last few months, they were severe. The case was studied clinically and roentgenographically until the death of the patient, following which a histopathologic examination was made. The studies justified the conclusion that the case was one of meningioma of the anterior cranial fossa with sarcomatous degeneration and invasion of the brain and the cranium. Salvator discusses Brissaud's views. Brissaud believed that the osseous changes are due to chronic irritation of the trigeminal nerve.

BERENS, New York.

ON SUPRASELLAR CHOLESTEATOMAS. HERBERT OLIVECRONA, Brain **55**:122 (March) 1932.

Two cases of cholesteatomas arising in the suprasellar region, with a variation in the chiasmal syndrome, are described. A diagnosis may be made preoperatively when there is slowly progressive primary optic atrophy with bitemporal hemianopia in a young person, a normal sella turcica, but widening of the optic foramina, pressure absorption of one or both anterior clinoids and absence of pituitary insufficiency. Cholesteatomas are congenital tumors, so that symptoms may occur at any age. Removal of the capsule and too much searching for the optic nerves are contraindicated because of the numerous herniations of the tumor into nearby clefts and crevices the anatomic relations of which are not clear.

MICHAELS, Boston.

PATHOLOGIC ANATOMY OF SO-CALLED EXPERIMENTAL POSTVACCINAL ENCEPHALITIS. HAROLD SCHMID, Encéphale **28**:337 (May) 1933.

This article reports experiments involving injections of smallpox vaccine both by the direct parietal route and through the orbit. Descriptions of the changes in ganglion and glia cells are given. However, conclusions are difficult to draw because, just as in all such experimental work, it is not possible to limit the zones of action of the invading material. Both meninges and brain proper will be involved in varying degrees—whatever the location of the injection. To account for limited actions the author assumes some kind of "hemato-encephalic" barrier, which can operate in a selectively defensive manner. At times this mechanism can "detoxicate" the virus or at least render it incapable of affecting the brain.

ANDERSON, Los Angeles.

PARATHYROID TETANY IN DOGS, AND ITS ABOLITION BY CURARE. H. HARTRIDGE and RANYARD WEST, Brain **54**:312 (Sept.) 1931.

For the most constant and valuable indicator of electrical hyperexcitability the authors used the cathodal opening contraction, which in tetany is reduced to about one-tenth its normal value. With the injection of curare into dogs with tetany there was no rise in electrical reactions unless the muscles were paralyzed by a very large dose of the drug. The electrical reactions rose coincidentally with the removal of the spasm when the tetany was abolished by parathyroid extract. There was no rise in the serum calcium when curare was given. Certain possible explanations of the action of curare in tetany are considered.

MICHAELS, Boston.

UNILATERAL REFLEX PUPILLARY CONTRACTIONS IN GLAUCOMA. G. N. BRAZEAU, Arch. Ophth. **9**:452 (March) 1933.

Brazeau describes a most unusual unilateral pupillary reflex phenomenon, which appeared in a patient during an iridectomy for glaucoma. The pupil first became long and narrow, then pyriform and then bulbous. After a few more minor contractions, all movements ceased and the pupil again resumed its normal state. The author states that it would be difficult to imagine anything more beautiful or

graceful than the pupil as it moved about, similar to a serpent. The author tries to establish some relationship between these unusual pupillary contractions and the sympathetic nervous system, but it is rather difficult to correlate the two.

SPAETH, Philadelphia.

CONTRIBUTION TO THE STUDY OF PARAPLEGIA IN POTT'S DISEASE. ETIENNE SORREL and MME. SORREL-DEJERINE, Rev. neurol. **1**:1, 1933.

This article is a review of the question of paraplegia from caries of the vertebrae based on a study of seventy-eight cases. While none of the observations and deductions are particularly new, several points of importance are stressed, particularly the fact that most of the paraplegias are due to the formation of an abscess, and that their eventual outcome is usually good under appropriate treatment. Persisting paraplegias are nearly always due to pachymeningitis, bony compression or severe vascular lesions. There are many excellent photographs of anatomic specimens illustrating the various types of lesions.

SCHNEIDER, Washington, D. C.

TREATMENT OF INFECTED WOUNDS OF THE BRAIN WITH BACTERIAL FILTRATES. J. R. B. BRANCH, A. A. LEMPERT and R. S. LYMAN, Arch. Surg. **28**:189 (Jan.) 1934.

In a study of the treatment of infected cerebral wounds in eight patients, the authors found considerable value in the frequent applications of a polyvalent streptococcus-staphylococcus filtrate to the dressings. Improvement in the appearance of the wounds was definite within four days, if at all, when the infection involved the surface of the brain and meninges and was widely exposed. The cases in which the wound failed to respond satisfactorily were instances of deep or disseminated infection of the central nervous system.

SPERLING, Philadelphia.

POLYNEURITIS DUE TO DIMETHYLENE ETHER OF ALLYL TETROXY BENZENE. A. NIKOLITCH and I. ALFANDARY, Encéphale **28**:116 (Feb.) 1933.

Ten case histories are abstracted from a series in the hospital at Belgrade. The patients were all women who had apparently taken dimethylene ether of allyl tetroxy benzene for the induction of abortion. Quantities, when ascertained, ranged from 1 to 9 capsules of 0.25 Gm. daily for periods up to several weeks. The findings are more or less typical of neuritides: atrophy of many muscle groups, corresponding loss of function, etc. Pain was noted in some instances. Varying degrees of recovery are noted: apparently all of the patients improved, but some were lost sight of before final observations could be made.

ANDERSON, Los Angeles.

SPONTANEOUS CEREBRAL VASCULAR ACCIDENTS IN DIABETES. WILLIAM R. JORDAN and PRESTON WATTERS, Am. J. M. Sc. **186**:488 (Oct.) 1933.

Cerebral vascular disease causes 7 per cent of all the deaths of persons with diabetes. Seventy unselected cases of cerebral vascular accidents are presented. The average age at the onset of the apoplexy was 62.2 years; there were fifty-two women and only eighteen men. Of the thirty-nine patients living, none is completely incapacitated. Arteriosclerosis was present in 91.4 per cent and hypertension in 70 per cent. In sixty cases the diabetes began before the apoplexy, with an average duration of six and three-tenths years prior to the apoplexy. In treatment, hypoglycemia should be avoided in such a condition as apoplexy.

MICHAELS, Boston.

EPILEPSY AND THE PARATHYROID GLANDS. G. LENART and EMIL VON LEDERER, Ztschr. f. d. ges. Neurol. u. Psychiat. **145**:655, 1933.

In an effort to determine a good method for the differential diagnosis of epilepsy from allied conditions, Lenart and von Lederer injected parathyroid extract (1 unit per kilogram of body weight) and observed the response of the eosinophils after an interval of five hours. It is possible in this way to differentiate definitely between epilepsy and hysteria. In epilepsy, including the jacksonian type, the variation in the number of eosinophils remains constantly less than 20 per cent; in hysteria, the variation is more than 30 per cent. ALPERS, Philadelphia.

HYPERVENTILATION IN NERVOUS DISEASES. A. BAUDOUIN and H. SCHAEFFER, Rev. neurol. **1**:445 (April) 1933.

The authors present a small series of cases, mainly of persons with epilepsy (thirty-five), in which hyperventilation was carried out. In about 15 per cent of persons with epilepsy typical fits occurred after five minutes. The authors point out that while the test is of little diagnostic importance in general, occasionally certain features of the fit pointing to possible cerebral localization may be observed. In a variety of other nervous diseases the changes following hyperventilation were negligible. SCHNEIDER, Washington, D. C.

LESIONS OF THE CENTRAL NERVOUS SYSTEM IN HERPES. RISER and SOL, Encéphale **28**:380 (May) 1933.

Two new clinical observations in herpes are presented—evidence of a diffuse celluloneuritis and an undoubted pyramidal syndrome. They followed some days after attacks of herpes, and careful examination failed to elicit other etiologic possibilities. Added to the published observations on hemiplegia, Landry's disease and other types of paralysis, encephalitis, etc., these cases constitute a further serious argument for the widespread diffusion of herpes virus in the central nervous system. ANDERSON, Los Angeles.

DO CENTRIFUGAL FIBERS CHANGING THE EXCITABILITY OF THE MUSCLES EXIST IN THE POSTERIOR ROOTS? E. T. VON BRUECKE and E. KRANNICH, Arch. f. d. ges. physiol. **231**:670, 1933.

Altenburger and Kroll described changes of the chronaxia in the gastrocnemius following stimulation of the peripheral ends of severed posterior roots. They assumed the existence of parasympathetic centrifugal fibers in the posterior roots acting on the muscles. The experiments of von Bruecke and Krannich contradict such a theory, as they failed to find any change of the chronaxia in the muscles with such stimulation of the posterior roots. E. SPIEGEL, Philadelphia.

THE ENDOCRINE EFFECTS OF CERTAIN OVARIAN TUMORS. EMIL NOVAK, Am. J. M. Sc. **187**:599 (May) 1934.

The important relationship of tumors to endocrine function is discussed. Granulosa cell tumors exert a feminizing influence through the production of estrogenic substance by the tumor cells. Hyperplasia of the endometrium associated with periodic bleeding occurs in older women. Arrhenoblastomas have a masculinizing tendency, probably because of their origin from undifferentiated epithelium in the region of the rete ovarii. The relationship to general problems of intersexuality, sex differentiation and sex reversal becomes apparent.

MICHAELS, Boston.

THE DEVELOPMENTAL PROFILE IN THE PRACTICE OF CHILD NEUROPSYCHIATRY. GEORGES D'HENCQUEVILLE, Hyg. Ment. **28**:101 (March) 1933.

The entire number of the journal is given over to presenting a technic applicable to the study of child neuropsychiatric problems. It is designed to be rapid and

to permit of interpretation at the time of study. It presents a series of tests of various functions: motor, sensory, verbal, etc., which can be put into graphic form against a more or less accepted normal. It is of greater prognostic than diagnostic value.

ANDERSON, Los Angeles.

NEURORETINITIS OF NASAL ORIGIN. P. BONNET and L. PAUFIQUE, Ann. d'ocul. **170**:606 (July) 1933.

Bonnet and Paufique observed a patient, aged 17, who for ten days had had vision of 1/30 and a wide central scotoma. Ophthalmoscopic examination revealed papilledema affecting one nerve, intense retinal edema and perivascular retinal exudates. Repeated coryzas, hypertrophy of the nasal mucous membrane and polypi and the absence of all general or serologic symptoms confirmed the conclusion that this case of neuroretinitis had its origin in the paranasal sinuses.

PULSATING EXOPHTHALMOS TREATED BY THE INJECTION OF GELATINIZED SERUM. P. BAILLIART and HERY, Ann. d'ocul. **170**:710 (Aug.) 1933.

Bailliart and Hery report a case in which pulsating exophthalmos of the right eye appeared after a cranial fracture. The patient was given ten subcutaneous injections of 80 cc. of gelatinized serum, with no relief. Doses of 160 cc. had to be given. The favorable result obtained seems to confirm the opinion that injections of gelatinized serum should be given before surgical treatment. There is no danger in giving these injections provided the material is sterile.

BLEPHAROSPASM AND HYSTERICAL AMAUROSIS. LAZARESCO and E. TRIANDAF, Ann. d'ocul. **171**:175 (Feb.) 1934.

Lazaresco and Triandaf observed a patient, aged 18, with menstrual disturbance, melancholia and suicidal tendencies. Marked blepharospasm of the right eyelid, right palpebral and periorbital anesthesia and right amaurosis were present. The patient could fuse with the stereoscope. Hypnotism and treatment with high frequency current completely cured the condition.

TUMOR OF THE OPTIC NERVE; EXTERNAL ORBITOTOMY AND RETROBULBAR EVISCERATION. P. BONNET, L. PAUFIQUE and A. LEVY, Ann. d'ocul. **170**: 540 (June) 1933.

A tumor of the optic nerve is described by Bonnet, Paufique and Levy. Histologically the tumor was an epithelial meningoblastoma. Roentgen rays showed an enlargement of the optic canal, which indicated that the tumor was situated deep in the orbit. After external orbitotomy the operation consisted of a true retrobulbar evisceration.

RESULTS OF ENDONASAL TREATMENT OF PITUITARY TUMORS. M. HIRSCH, Ann. d'ocul. **170**:692 (Aug.) 1933.

Hirsch describes his transseptal method of operating on pituitary tumors and illustrates by means of photographs the various forms of these tumors. He used this method in operating on 233 patients and obtained remarkable results. He observed 57 of the patients for from four to thirteen and one-half years after operation and found that 41 showed improvement without relapses.

KENNEDY'S RETROBULBAR NEURITIS IN THE DIAGNOSIS OF FRONTAL TUMORS. G. DE NIGRIS, Ann. d'ocul. **170**:704 (Aug.) 1933.

De Nigris discusses Kennedy's retrobulbar neuritis observed as an early symptom of a large *lymphangiothéliome*, situated on the right lesser wing of the sphenoid. He stresses the importance of this early symptom in the diagnosis of fronto-orbital tumors which compress the frontal lobe.

POLYMORPHOUS HEREDITARY SYPHILITIC LESIONS OF THE EYE OBSERVED IN THREE BROTHERS. J. ROLLET, Ann. d'ocul. **170**:542 (June) 1933.

Hereditary syphilitic lesions of the eye were noted in three brothers; the two older ones had interstitial keratitis; the second child also had unusual peripapillary lesions, which were observed likewise, in the third. In addition, the third brother had Argyll Robertson pupils.

HEADACHE OF NASAL ORIGIN. SARGNON, Ann. d'ocul. **170**:699 (Aug.) 1933.

Sargnon devoted careful and critical study to headaches of nasal origin. He states that they are due to acquired lesions, particularly to anterior ones, such as traumatic, inflammatory, nervous or neoplastic lesions. He discusses the etiology and symptomatology of these lesions in relation to medical and to surgical treatment.

HYPOPHYSEAL DISTURBANCES IN CASES OF CHRONIC SINUSITIS AND PERISINUSITIS. M. SILVAGNI, Ann. d'ocul. **170**:698 (Aug.) 1933.

Silvagni studied the relation between hypophyseal function and chronic sinusitis. Hypofunction of the hypophysis was noted, but its action after intervention has not been studied thoroughly because sufficient time has not elapsed.

HALO OBSERVED IN CASES OF ARTERIAL HYPOTENSION. GALLOIS, Ann. d'ocul. **170**:534 (June) 1933.

Gallois reports three cases in which neither glaucoma nor ocular hypotension was present, though the patients saw halos around lights. Mawas stated that halos are frequently seen by patients with incipient cataract.

NEURITIS DUE TO ALCOHOL AND TOBACCO AND MORPHOLOGIC CHANGES IN THE NOSE AND SINUSES. E. MORELLI, Ann. d'ocul. **170**:697 (Aug.) 1933.

Morelli observed morphologic changes in the nose and in the sinuses in cases of neuritis due to alcohol and tobacco.

BERENS, New York.

Society Transactions

PHILADELPHIA PSYCHIATRIC SOCIETY

Regular Meeting, May 18, 1934

JOSEPH C. YASKIN, M.D., *President, in the Chair*

JUVENILE DEMENTIA PARALYTICA: REPORT ON A SERIES OF CASES. DR. SAMUEL COHEN and DR. ROBERT S. BOOKHAMMER.

We have studied the results obtained from treatment in 10 cases of juvenile dementia paralytica seen at the Philadelphia Hospital for Mental Diseases. Nine of the patients received tryparsamide intravenously; in addition to the tryparsamide, 2 of them received malarial therapy and 2, diathermy. One other patient received a bismuth preparation in addition to tryparsamide. The tenth patient received malarial therapy only.

Four patients improved sufficiently to leave the hospital, 3 becoming self-supporting. Of those remaining in the hospital, 2 have shown definite improvement, 1 has had insufficient treatment to permit any conclusions to be drawn, and the other 3 have not been benefited. Intensive therapy with tryparsamide is recommended, with the additional use of malaria or diathermy when possible.

DISCUSSION

DR. HAROLD D. PALMER: I have observed about 12 cases of juvenile dementia paralytica, and I must admit that the possibility of obtaining such favorable results through treatment has not occurred to me. I looked up the records of cases in the outpatient department this afternoon. The first patient was seen at the age of 8 years. The father was undergoing treatment for dementia paralytica at that time in the Graduate Hospital of the University of Pennsylvania and is now a patient in the Philadelphia Hospital for Mental Diseases. The mother had a condition that also had been diagnosed as dementia paralytica and was receiving antisyphilitic treatment. A sister also had juvenile dementia paralytica, and follow-up notes state that she died within a year after examination. The third patient who had been treated with tryparsamide showed considerable physical improvement, but the condition progressed to dementia. I am sure that at least 2 of the patients might have been distinctly benefited by the treatment which Drs. Cohen and Bookhammer have outlined in their paper. I believe that the article by Potter in 1933, referred to in this paper, contains the only optimistic note that has ever been published in favor of treatment for juvenile dementia paralytica. Potter stated that of 60 patients, 38 received malarial therapy, tryparsamide or both. In 27 of the 38 cases the treatment was effective in preventing further deterioration. Five patients had complete remissions, and 9, partial remissions. Potter believed that the prognosis is best in cases in which the patient was of normal mental status prior to the onset of dementia paralytica and was past adolescence when the symptoms developed, and in which the time between the onset of the disease and treatment does not exceed two years. He believed that the treatment of choice is that with malaria and tryparsamide.

The paper by Potter emphasizes another important point, that cases of mental deficiency should be more carefully studied, with routine Wassermann tests of the blood and spinal fluid. One excellent feature of the clinical and laboratory studies in the psychopathic department of the Philadelphia General Hospital is routine examination of the spinal fluid. The most remarkable thing brought out in the paper by Drs. Cohen and Bookhammer was that following treatment 3 of the patients were able to earn a living. It might be worth while to emphasize

that in cases of dementia paralytica in persons in the early twenties more carefully taken family histories might rule out the possibility that the juvenile dementia paralytica may be associated with congenital syphilis rather than rapidly developing so-called acquired dementia paralytica. Perhaps in cases in which a diagnosis of dementia paralytica has already been established one is too ready to accept as evidence of acquired syphilis the simple statement that a sore appeared on the genitals in early adolescence.

DR. S. F. GILPIN: The accurate diagnoses reported as having been made in the psychopathic department are a comfort to me. I have not treated patients with juvenile dementia paralytica in private practice, but all the patients with whom I have come in contact in the hospital have presented so much mental loss that I considered treatment to be useless. When I believe that the disease has been in existence too long and that the organic changes are too great I do not feel justified in giving treatment. Although the Wassermann reaction may be negative, the patient is crippled mentally, and life means little to him. It is a question how far advanced the disease is in each patient, and that is often a hard point to decide.

I notice that the end-results reported by Drs. Cohen and Bookhammer in their series of cases are about the same as those in cases of acquired dementia paralytica. The great trouble so often is that an early diagnosis is not made in cases of dementia paralytica. If a child is born with syphilis it is not known, in many cases, how far dementia paralytica has developed before mental symptoms are shown. The discouraging feature is that however good the response to treatment the mental loss may be marked.

DR. JOSEPH C. YASKIN: I have observed several cases of juvenile dementia paralytica in the past two years; in the last, Schilder's disease was diagnosed first. The final diagnosis proved to be juvenile dementia paralytica. The first patient was seen by a number of physicians at the Philadelphia General Hospital. He had an unusual form of striatal disturbance. Pathologic examination left no doubt that the condition was congenital syphilis. In both of my cases the blood and the spinal fluid have been negative for syphilis.

PARANOID DEMENTIA PRAECOX INFLUENCED BY PRIMARY ANEMIA. DR. WILLIAM H. IZLAR (by invitation).

Mental changes in cases of pernicious anemia have been neglected and are briefly dismissed in most textbooks under the description of the disease. The usual reference to mental change is: "As the disease progresses there may be great depression, sometimes delusions, but mental symptoms, as a rule, are not marked." In the original description of pernicious anemia, Addison referred to "occasional wandering and indeed a terminal delirium." Mental symptoms occur more frequently in this disease than is generally recognized. Langdon drew attention to a group of cases in which nervous and mental symptoms may precede a typical picture of pernicious anemia. Of the mental changes that he noted, peevishness and gradual mental deterioration, varied by periods during which the patient more or less returned to normal, were the most common. Pickett reported 6 cases. Among the mental symptoms he noted was a shallow confusion with impairment of ideas of time and space. Delusions, especially of a persecutory character, he believed to be common. In a review of 11 cases by Barrett the commonest symptoms were delusions of persecution, sometimes systematized, disorientation in time and space and irritability; there was little mental deterioration. McAlpine stated recently that mental changes occur not uncommonly in cases of pernicious anemia; they range from a state of depression to a definite psychosis.

The case to be presented here is that of E. H., aged 44, a white woman, single, a typist, who was admitted to the Philadelphia Hospital for Mental Diseases on April 9, 1929. The patient's father died of cancer of the stomach. The mother died of heart disease and nephritis at the age of 39. A brother and a sister died of tuberculosis. A nephew had epilepsy. The patient had scarlet fever and

measles and has suffered from violent abdominal pain since childhood. She has always been of a retiring disposition and made few friends. In 1927 the patient noticed that she would feel tired out after the least exertion. There was an increasing indisposition to physical activity. The heart was readily made to palpitate; there was a tingling in the upper extremities and it was impossible for the patient to carry packages because the arms ached and felt tired. She would walk with her hands on the lapels of her coat to relieve the pain. She became irritable and hard to get along with; she suffered from severe nausea and vomiting associated with diarrhea and abdominal pain. Hysterectomy and appendectomy were performed. During the patient's last week in the hospital delusions of persecution and auditory hallucinations developed, and she became extremely paranoid in her attitude toward the personnel. At this time also there was severe anemia (the red cells numbered 1,560,000; the hemoglobin was 35 per cent, and the color index, greater than 1). The blood picture greatly improved after two blood transfusions, the red cell count increasing to 3,600,000 and the hemoglobin to 79 per cent, but there was no corresponding improvement in the mental condition. The knee jerks and achilles tendon jerks were absent. It was at this stage that the patient became unmanageable and was referred to the Philadelphia Hospital for Mental Diseases.

When the patient was first seen her bulkiness and the amount of obesity presented a striking contrast with her ghastly pallor. The mucous membranes were extremely pale; marked glossitis was present, and the tongue was extremely tender. The blood pressure was 78 systolic and 40 diastolic. The right lower extremity appeared shortened owing to the fact that the patient would not flex the knee. The hands were short and stubby, and the nails showed transverse ridges with extremely pale nail beds. The knee and achilles tendon jerks were absent on the left side and diminished on the right. Blood studies at this time showed: red cells, 800,000; white cells, 5,000; hemoglobin, 30 per cent, and color index, 1.8. The erythrocytes showed so-called punctate basophilia, and a remarkable degree of anisocytosis, poikilocytosis and polychromatophilia. Gastric analysis showed absence of free hydrochloric acid and a low total acidity.

The mental symptoms at this time were marked. The patient was difficult to handle. She had frequent crying spells, was constantly fighting and was extremely hostile, restraint being necessary. She harbored many delusions of persecution, had hallucinations of an auditory nature and maintained an extremely paranoid attitude toward the personnel of the hospital. She would write on an average ten letters a day to the President, governor and mayor, criticizing the institution. She was oriented in all spheres, but her judgment, reasoning and insight were greatly impaired.

Liver therapy was begun, 1½ pounds (680.4 Gm.) of liver being given daily, with ½ drachm (1.85 cc.) of dilute hydrochloric acid before and after meals. There was a steady and continuous improvement in both the physical and the mental condition. Nausea and vomiting ceased; the glossitis and the pain in the extremities disappeared. After four months of treatment the red cells numbered 4,000,000; the hemoglobin was 84 per cent, and the color index was still greater than 1. The blood pressure at this time was 122 systolic and 78 diastolic. Gastric analysis still showed absence of free hydrochloric acid and a low total acidity. The knee and achilles tendon reflexes were present and active bilaterally. Mental improvement was great. The irritability was lost; crying spells had ceased, and the hostility had given way to friendliness. The auditory hallucinations disappeared. There was an abrupt ending to letter writing, and the patient became helpful about the ward. However, she retains the paranoid ideas, but does not burden others with them.

Soon after admission the patient received an alleged injury to the right knee while being restrained. Following this accident she held the knee stiff and cried out with pain at any attempt made to flex it. For a year she walked only with the aid of crutches. After some improvement in the general condition the knee was examined; roentgenograms showed a normal picture, and there were no arthritic changes, disease of the bone or injury. Sodium amytal was given intravenously, and the knee was then flexed and put in a plaster cast. The cast

was removed two days later, and the patient was told that she would now be able to walk and run. She at once used the extremity without the aid of crutches.

This case presents a clear picture of primary anemia preceding the development of a psychosis. The mental symptoms became less marked with improvement in the physical condition following liver therapy. This at once brings up the question as to what part the pernicious anemia played in the etiology of the psychosis. Is there a psychosis associated with pernicious anemia? I do not think that there is, but this case clearly shows a psychosis with improvement in the mental condition accompanying improvement in the blood picture.

DISCUSSION

DR. SPURGEON O. ENGLISH: This stimulating paper brings up one of the important problems in psychiatry concerning etiology. The incidence of psychoses in cases of pernicious anemia varies from 4 to 15 per cent. In explanation one sees two opposing points of view: (1) that a specific toxin or neuropathologic change exists or (2) that the mental change is merely incidental to the disease and perhaps precipitated by the more difficult life situation in which a patient with such a serious disease is placed. It seems, however, that the incidence of psychosis in cases of pernicious anemia is a trifle too high to be accounted for by incapacity alone. Other chronic diseases such as tuberculosis do not show such a high incidence, even though any disease or condition which threatens dissolution of the ego may precipitate regression. Hackfield, in 1933, argued that if neuropathologic changes occur one cannot have recovery or improvement. However, in manifestations due to disease of the spinal cord one does see functional if not organic improvement following treatment. Does something analogous take place in the mental sphere, and can this be due to temporary lack of oxygenation as seen in cases of psychosis following carbon monoxide poisoning with recovery? This may be a problem for the neurophysiologist. In Dr. Izlar's case improvement did not occur after transfusion, but did occur after liver therapy. Does this mean that the improvement in the blood picture was not sufficiently permanent after transfusion?

DR. HAROLD D. PALMER: I am sure that if one looks for a specific psychopathology in cases of pernicious anemia one will not find it. I recall seeing manic-depressive, schizophrenic and catatonic manifestations in a small group of patients at the Philadelphia General Hospital and the Pennsylvania Hospital. I am more inclined to think that the occurrence of the anemia is not related etiologically to the mental disease, except as it can be considered one of the factors reducing the patient's total psychic resistance. This point of view is supported by the fact that relief of the physical illness brought about through intensive liver therapy failed to alter the course of the paranoid reaction. I had an opportunity to study the cases reported by Hackfield in his recent contribution from the Pennsylvania Hospital. As I recall it, one of his major points and primary purposes in this paper was to refute the idea of a specific psychosis in cases of pernicious anemia which seems to have grown up in the literature. Woltman, of Rochester, Minn., in a paper a number of years ago seemed to imply that there was something specific about the psychotic reaction of a series of patients with pernicious anemia and mental disease. Let me cite a case: I recently saw a patient at the Pennsylvania Hospital who had been admitted first in 1924 with a catatonic schizophrenic syndrome. She was physically ill and had a temperature of 103 F.; the condition was finally diagnosed as acute mastoiditis, and an operation was performed. Recovery from the surgical operation was accompanied by recovery from the mental illness, and at the end of two or three months the patient returned home and took up an apparently normal life. She remained well for four years and was able to hold a position in a store in New Jersey. In 1928 she was again admitted to the hospital, presenting the same catatonic schizophrenic picture, this time without any physical precipitating factors. She has remained mentally ill since the second admission. What I wish to emphasize in citing this case is that any person predisposed in early life to mental illness may be abruptly precipitated

into a psychotic episode by physical disease. It seems to me that in such cases the physical disease or toxic process is merely an incident in the career of a person predisposed to mental disease. I note that the title of Dr. Izlar's paper, "Paranoid Schizophrenia Influenced by Primary Anemia," expresses just this point of view, that the paranoid schizophrenic reaction represents the primary illness and is merely influenced incidentally by the development of pernicious anemia.

DR. JOSEPH C. YASKIN: It is difficult to reconcile a psychotic reaction of this type, i. e., a definite paranoid reaction, with an organic psychosis. In psychoses associated with anoxemia the reactions are usually entirely different, being associated with disorientation and other evidences of an organic psychosis. I should, therefore, be loath to refer the paranoid reactions of this type to the anoxemia of pernicious anemia. I should rather look for the explanation of the paranoid trend in the prepsychotic history of this patient.

DR. A. C. BUCKLEY: I have seen pernicious anemia associated with psychoses. I have also seen cases in which the psychotic state was apparently due to pernicious anemia and in which with the improvement of the anemia the mental condition improved. Dr. English's point of view is rational. I do not know any way of improving on it. I know of a woman, aged 78, who is in the terminal phase of schizophrenia. The mental condition has been stationary for about thirty years. Two months ago edema of both hands and the face appeared. My associates and I were much surprised to find the hemoglobin 20 per cent, and the red blood cell count less than 2,000,000, with nucleated red cells and the usual characteristics of pernicious anemia. The patient was given massive doses of liver, with iron and ammonium citrate; today the hemoglobin is 75 per cent, and the red cells number 3,000,000. The physical condition appeared to have no influence whatever on the mental symptoms.

DR. FRANK R. STARKEY: Not much is known about the relation of organic conditions to various psychotic reactions. I do not think that one is justified in stating that a definite type of psychosis can be attributed to primary anemia. Most cases of primary anemia reveal no psychosis whatever, even though there are definite organic changes in the nervous system; they are usually situated mainly in the spinal cord and do not affect the mental processes. One interesting feature about psychiatry is that one sees the same reactions at times in any of the organic manifestations from trauma to dementia paralytica and also these same phenomena in cases in which no definite organic pathologic change is revealed. The type of reaction may change from day to day, running the entire gamut through what one may term hysterical, hypochondriac, manic-depressive and schizoid manifestations. These constellations should be looked on not as distinct entities but rather as reactions which may vary from time to time and, as I have said, may occur with or without organic changes.

DR. WILLIAM H. IZLAR: In reply to Dr. English, for a little over a year the blood picture remained improved after the transfusions, and during that time the mental symptoms showed no change. Since the blood count has increased in response to a liver diet for two years and during that time improvement has been noted in the patient's condition, I feel that the liver therapy is the better treatment. A noticeable improvement occurred in four months; the red cell count rose from 800,000 to almost 4,000,000.

TUBERCULOUS MENINGITIS: RECOVERY WITH NEUROPSYCHIATRIC SEQUELAE: REPORT OF TWO CASES. DR. ROBERT A. MATTHEWS and DR. SAMUEL ZERITSKY.

Tuberculous meningitis is encountered most frequently in children but has been reported at all ages. Although less common now than formerly because of the lowered prevalence of all forms of tuberculosis, it is by no means rare. The disease is generally fatal, but rare cases of recovery have been reported by reliable authorities, In 1922, Cramnar and Bickel collected 46 such cases. Others have been reported since.

Within the past year, 2 patients who had presumably had tuberculous meningitis were admitted to the Philadelphia Hospital for Mental Diseases. Both had recovered from the meningitis but had serious mental defects of a similar nature. One patient has since died, and an autopsy was performed. The other is still living and will be presented this evening.

CASE 1.—J. L., a white man aged 60, formerly employed as a dishwasher, was admitted to the medical ward of the Philadelphia General Hospital on Sept. 25, 1933. According to the meager history given by the woman in whose home he had lived for the previous five years, he had always seemed sensible but at times drank heavily, although he never became troublesome. On learning that he had not left his room for three days she investigated and found him in such an acutely ill condition that he was unable to respond to questions.

When admitted to the ward the patient was stuporous, and his breathing was of the Cheyne-Stokes type. The temperature was 100 F. (axillary), the pulse rate, 92, and the respiratory rate, 40. There were marked nuchal rigidity, a bilateral Kernig sign and evidence of involvement of the lower lobe of the right lung. The general physical condition was poor, and the man was undernourished to the point of emaciation. A spinal puncture yielded clear fluid with a cell count of 100, all lymphocytes, and a trace of globulin.

During the next few weeks there continued to be a low grade elevation of temperature, centering about 100 F. Numerous examinations of the spinal fluid were made, with consistent results. Positive reactions were obtained to the tryptophan and Levinson tests, and at all times there was pleocytosis, with a marked preponderance of lymphocytes. The amounts of sugar and chloride, however, were within normal limits. Although tubercle bacilli were not demonstrated on smear, inoculation of a guinea-pig with spinal fluid produced characteristic tuberculous lesions.

Treatment consisted of repeated drainage of spinal fluid and injection of lesser quantities of air, the introduction of Pregl's solution (the solution resulting from the action of iodine on sodium carbonate) by the carotid artery and the intravenous administration of dextrose. The patient's temperature became normal in two weeks, and he was considered convalescent in a month following admission, but it became necessary to transfer him to the psychopathic ward because of irritability, pugnacity and a confused mental state.

Two weeks following the transfer, another low grade febrile reaction developed, and the temperature remained above normal for a month. Following this, the physical condition improved but the mental state, characterized by confusion and dementia, remained unchanged. He was committed to the Philadelphia Hospital for Mental Diseases on Jan. 4, 1934. While there no evidence of meningeal irritation was elicited. He became extremely filthy in habits; pressure sores developed, and he died of bronchopneumonia on March 17.

Autopsy confirmed the diagnosis of bronchopneumonia. The brain was examined by Dr. Alpers, who will present the pathologic changes in his discussion of the case.

CASE 2.—P. N., a white married man aged 57, a baker, was admitted to the neurologic department of the Philadelphia General Hospital on March 23, 1933, with a history of periods of drowsiness and dull pain in the right side of the head for about a month. He had been out of work since 1930 but prior to that had been steadily employed by the same concern for twenty-five years.

When admitted to the hospital, the patient did not appear to be acutely ill but could walk only with great difficulty. Neurologic examination gave essentially negative results except for generalized hyperreflexia. No pathologic reflexes were noted. A diagnostic spinal puncture yielded turbid fluid containing 930 cells, of which 90 per cent were lymphocytes, and a cloud of globulin. A smear for tubercle bacilli gave negative results. A roentgenogram of the skull revealed increased density of the right parietal region, the significance of which is still uncertain. Further studies of the spinal fluid showed positive reactions to the tryptophan and Levinson tests. There was an extremely low sugar content, varying from 5 to 15 mg. per hundred cubic centimeters, and the chlorides measured

674 mg. The Wassermann and Kahn reactions of the blood and spinal fluid were negative, but there was a high first zone colloidal gold curve.

Drainage of the spinal fluid was done six times at weekly intervals, and mercury and iodides were administered. Because of a purulent nasal discharge a careful survey, including roentgenographic examination of the sinuses, was made. The frontal, ethmoid and maxillary sinuses were found to be infected; they cleared up under appropriate treatment. During this period the temperature remained normal, and there was considerable improvement in the mental condition, but the gait continued to be impaired. In May the patient was discharged from the hospital, only to be readmitted in June with the same complaint of inability to use the lower extremities. A suggestive bilateral Kernig sign was present. Again drainage of the spinal fluid was performed at weekly intervals, and it was noted that occasionally the needle became clogged with a whitish exudate. Inoculation of guinea-pigs with the spinal fluid showed no evidence of tuberculosis, but there was still pleocytosis.

Owing to the patient's mental confusion, irritability and restlessness he was transferred to the psychopathic department, where he remained until September, when he left the hospital against advice. There was no improvement in the condition while he was at home, and it is stated that he had to be cared for "like a baby." In October he was again returned to the psychopathic ward and was subsequently committed to the Philadelphia Hospital for Mental Diseases on October 19. During the several periods of hospitalization the patient's temperature remained within normal limits except for three febrile phases of two days' duration each, when it mounted to 101 F.

Since admission to this hospital the patient's physical and mental condition has remained essentially the same. He is somewhat undernourished and is confined to bed or a wheel chair because of inability to walk. He has some difficulty in assuming a standing position, but once in an erect posture his station is good. However, he is not able to walk unaided, and any attempt at voluntary locomotion results in a few shuffling steps with a tendency to propulsion. While he is in bed he is able to move all his extremities voluntarily. The tactile, pain and temperature senses as well as the proprioceptive sense are retained. The patellar and achilles tendon reflexes are definitely exaggerated, but there are no pathologic reflexes. Plantar irritation on the left seems to produce an indefinite dorsal flexion of the great toe, which is difficult to evaluate because a portion of the hallux has been amputated.

There is some difficulty in communicating with the patient owing to his faulty English, yet occasionally his responses are surprisingly clear, proving that he does comprehend to some extent. Although apathetic, he is respectful and attempts to cooperate, but there is rapid mental tiring. After answering a few questions intelligently he appears to become confused, and his responses show stereotypy. It is thought that this may be an aphasic manifestation.

DISCUSSION

Dr. Bernard J. Alpers: Cases of chronic tuberculous meningitis are rare, but they have been reported, especially in adults. There seems to be good evidence in the first case that there was a tuberculous infection, for the guinea-pig test was positive. Study of the brain revealed meningo-encephalitis. The meningeal infiltration was composed almost entirely of lymphocytes, but there was no evidence of miliary tubercle formation. There was definite arteritis. Thus far I have been unable to demonstrate tubercle bacilli in the exudate. However, I am inclined to believe that the meningitis is of a chronic type, possibly tuberculous in origin, though it is not of the type ordinarily seen in this disease.

Dr. Joseph C. Yaskin: Dr. Alpers is fully aware of the fact that many cases of tuberculous meningitis are terminal processes of a general miliary tuberculosis. I should be loath to make a diagnosis of tuberculosis of the central nervous system if at autopsy I could not find a trace of the primary lesion in the hilus of the lungs, in some of the glands or elsewhere.

MANIC-DEPRESSIVE PSYCHOSIS WITH CATATONIA. DR. JOHN WARD (by invitation).

In studying patients who present catatonic phenomena, one naturally thinks first of the schizophrenic group. It is well known, however, that these symptoms occur also in the manic-depressive group. At least they have been so described by Bleuler, Strecker and Ebaugh, White, Hoch and many others. In a large group of cases my associates and I have found few patients with manic-depressive psychosis who present true catatonic states. With this in mind, the case which I shall present now will, I believe, afford an interesting subject for discussion from the standpoint of diagnosis and prognosis.

M. R., a white woman, aged 36, divorced, is the daughter of a father who died at 63 years of age of nephritis, and a mother who is living at 70. There are 6 sisters; 1 (Gertrude) died in the Norristown State Hospital after fifteen years' residence; 1 (Elizabeth) has been a patient in the Philadelphia Hospital for Mental Diseases for the past fourteen years, her condition being diagnosed as manic-depressive psychosis. Elizabeth has been out on parole for only one short period in fourteen years and has shown gradual but steady intellectual deterioration. I believe that her condition is dementia praecox. Of the remaining 4, 2 sisters died at an early age and 2 seem normal. Three brothers have not shown any psychotic symptoms. An uncle committed suicide and was believed to be psychotic. The patient has 2 children, a boy aged 18 and a girl aged 17; both are healthy.

The patient was born in Philadelphia in 1898. Her childhood was normal as far as is known. She finished grammar school and took a business course. She had hosts of friends of both sexes and went to many parties. She was an excellent pianist. Much of her time was spent in caring for her invalid mother. At the age of 17 she was seduced, and a forced marriage followed. In the first three years of married life she had 2 children and is said to have been extremely unhappy. The husband was cruel and often beat her; he was very lazy, seldom working, and had affairs with other women.

At the age of 20 the patient contracted influenza, during which she had little treatment and inadequate care. Following recovery she became depressed, agitated and self-accusatory, and hospitalization became necessary. In December 1918 she was admitted to the Friends Hospital in a depressed and agitated state; she attempted suicide there by swallowing various small articles. She thought people were trying to murder her children. She constantly tried to disrobe; she masturbated freely and was markedly confused and had hallucinations. At the end of four months she became mute and catatonic, and in this state she was taken home.

Six months after being removed from the hospital she is said to have returned to her prepsychotic state. During this interval her father died, but the patient was little affected by this. She was granted a divorce from her husband in 1922. About this time she was troubled with an anal fissure and had two or three operations. In 1926, at the age of 28, she secured a position with a railroad company as a clerk. She worked at this for three years and was said to be well adjusted and happy. In 1931 she stopped work because of the illness of her mother. The following year she started proceedings in court to force her ex-husband to support his children. Soon after this she became depressed, spoke constantly of the court proceedings and seemed to worry considerably over the accusations she had made against her husband. In January 1933 she was so agitated and depressed that she was unable to sleep; she cried and moaned and rolled on the floor, claiming she had been poisoned. Hospitalization again became necessary.

She was admitted to the Philadelphia General Hospital and then committed to the Philadelphia Hospital for Mental Diseases on Feb. 7. On admission she was depressed, agitated, apprehensive, tearful and self-accusatory. Judgment and insight were markedly impaired, though she was well oriented and her memory was good. She weighed 188 pounds (85.3 Kg.), and examination showed her to be in good physical condition except for mild cervicitis and secondary anemia. The mental state remained unchanged for about three months. During this time she was in continuous tub baths on several occasions; she lost considerable weight.

Four months after admission she had a short period of about three weeks when she was quiet and lucid. She soon became agitated and fearful again, and at times noisy. The usual sedatives seemed to have little effect, and she became progressively worse until February 1934. At this time she weighed 113 pounds (51.3 Kg.), having lost 75 pounds (34 Kg.). She was treated with generalized ultraviolet irradiation, and the condition seemed to improve somewhat.

In March she was paroled to the custody of her family but was brought back the next day in a highly agitated and disturbed state. Since then she has been catatonic. For several weeks she remained sitting motionless in bed, staring straight ahead and occasionally mumbling incoherently. At present she walks about her room, feeds herself and occasionally steals other patients' food, but she remains resistive and at times definitely cataleptic. She is gaining weight slowly; at present she weighs 117½ pounds (53.4 Kg.) and the general physical condition seems much improved.

DISCUSSION

DR. A. C. BUCKLEY: There are no more important differentiations than those involving the question of the schizophrenic manic-depressive psychoses. From the clinical and the economic standpoint it is of the utmost importance to determine whether or not the patient is likely to need the care of the hospital during the remainder of her life. A number of such difficult cases present themselves from time to time which call for careful study before a diagnosis and prognosis can be reached. If one adheres to certain fundamental symptomatologic standards, one thinks of the symptom hallucination as being always present at one time or another in the schizophrenic person. In cases of pure mania, this symptom is absent. Next one must consider the emotional content. The schizophrenic emotional reactions are paradoxical and inconsistent; the patient often appears to be acting a part rather than portraying real emotional states, while in the manic-depressive psychoses the patient faithfully portrays emotions and expresses them in his behavior. Dr. Ward mentioned that the catatonic symptom complex is not pathognomonic of any particular form of disease. Catatonia has long been known to occur in many types of disorder. Kahlbaum emphasized this fact in his monograph "Die Katatonie" written in 1873. Profound depressive states resembling catatonia also occur in cases of epidemic encephalitis, in cases of schizophrenia and especially in cases of depression in middle-aged persons. This patient's mental condition came on a few months after a severe illness that was diagnosed as influenza. She was in poor physical condition for a time during which she certainly passed through a state of marked confusion with evidence of hallucinations, as far as one could tell. One sometimes thinks that patients are hearing outside voices when they entertain intensified ideas. This patient appeared to react to auditory hallucinations. She said that she saw persons who were going to murder her children, and I notice a note in the summary of the case that when no one was near she would call out not to harm her children. She also said that she knew those persons did not like her and were sticking pins in her. A provisional diagnosis in this case was postinfluenzal toxic psychosis of the manic-depressive type, which, however, was not verified. The patient was taken out of the hospital at the end of four months, with no evidence of improvement.

In the ordinary case of toxic psychosis improvement is usual at the end of four months. One also sees young people who pass through psychotic episodes, having attacks of manic or depressive psychoses. Very often there is an interval of normal mental life for years and then a recurrence either of depression or of excitement. Perhaps recovery from that attack may occur, followed by another recurrence, and then the course is downward. There may be continued depressions of longer duration, the patient remaining in the hospital for perhaps a few years. W. R. Dunton a few years ago wrote of cyclic forms of dementia, bringing out the similarity of some of these to so-called manic-depressive states. I neglected to state that a number of years ago I reported the case of a man, aged 50, with involution melancholia, who passed into a state of catatonia

in which he remained for a year. He was rigid from head to foot and could be carried like a log. Dr. Kirby and others also have reported similar cases occurring in persons in middle life.

DR. S. F. GILPIN: The differential diagnosis between manic-depressive psychosis and schizophrenia, when one first sees the patient, is at times difficult. Both psychoses begin early in life and usually begin with depression. However, there is a difference in the two conditions which is well marked after sufficient data have been obtained. To me the manic-depressive psychosis is a definite, clearcut condition. It does not partake of the symptoms of any other condition so much as to render diagnosis difficult. It does not occur in such a family history as was obtained in this case. Many people in this family have been hospitalized and have not recovered; this does not occur in manic-depressive families. When one examines the patients in this family group he finds them deteriorated mentally; in the case of dementia praecox that ends in recovery and permanent mental health the diagnosis is open to suspicion. After the fourth or fifth attack the patient is ready for years of hospitalization. This is not so in cases of manic-depressive psychosis. These patients may go through a lifetime of recurrent attacks with periods of normal mentality between. They usually come from the "upper ten" mentally; the most brilliant people come from the manic-depressive group. Schizophrenic patients come from an entirely different group; as a rule they do not belong in brilliant family groups. There is often the history of physical disease, such as tuberculosis, syphilis or alcoholism, and of other causes of germ plasm degeneration in these groups.

As I listened to the description of the family history and the past medical history in this case it does not seem to be possible to consider manic-depressive psychosis.

DR. JOHN WARD: On admission to the Philadelphia Hospital for Mental Diseases this patient presented the typical picture of agitated depression common in manic-depressive psychosis. The history is that she had fully and completely recovered from the first psychotic episode and was an intelligent girl. These facts led to the diagnosis of manic-depressive psychosis. When she became catatonic, even though I realized that catatonic states occur in many of the psychoses, I began to suspect that the diagnosis was wrong. Careful investigation of the family history brought out the facts which, as Dr. Gilpin stated, point so strongly to a diagnosis of schizophrenia. In view of these facts I believe that the diagnosis in this case will have to be changed to dementia praecox of the catatonic type.

CHICAGO NEUROLOGICAL SOCIETY

Annual Meeting, May 19, 1934

PERCIVAL BAILEY, M.D., *President, Presiding*

NEURASTHENIA WITH OBSESSIONS. DR. CLARENCE A. NEYMANN.

P. F. B., a man aged 29, was first seen on Jan. 20, 1932, when he complained of many fears and doubts as to his ability to do anything. He was in the automobile supply business and had had to stop work because he could not talk to customers on account of the fears. He often ran away when a customer approached him. He was so self-conscious that he could not go out and enjoy himself. The self-consciousness was especially evident in a barber shop, and for this reason he had not had his hair cut for many months. He had not left the house for several weeks because of fears of facing people and because of a pronounced feeling of depression.

Psychoanalysis, extending over two years, revealed a masturbation complex from which the patient had been suffering since the age of 16 (he had been informed

that he would go insane) and an Oedipus fixation and fear of castration. The fixation had been so strong in childhood that he could not go to sleep before his mother had retired, and he watched for her at a window whenever she left the house until she returned. The mother was evidently neurotic and early taught him that any mention of sexual matters was taboo. When a younger brother asked her about childbirth, she insisted that they all kneel down and pray, and she sprinkled holy water over the children. She used scissors nightly to clip the patient's nose with the laudable purpose of removing a wart. An older brother burned his hand while sliding down a rope and was taken to a hospital, where he was circumcised. The patient interpreted this as punishment for the sexual pleasure derived from sliding down the rope, a pleasure which he had often experienced. All this occurred at about the age of 6, and resulted in a fear of circumcision and castration. He also had an oral fixation, which centered on his weaning. In place of the breast his mother presented him with a homemade indoor ball, covered with leather from her gloves, when he was 3 years old. As a child he continued to symbolize this ball as the mother's breast and never wished to be parted from it. He also drank from the nursing bottle of the younger brother until the age of 4 and from this derived great satisfaction.

The analysis is too long and complicated to reveal all its details and side issues. The patient has now been at work for over a year and has abandoned most of his fears, phobias and obsessions.

DEMENTIA PARALYTICA, GRANDIOSE TYPE. DR. CLARENCE A. NEYMANN.

H. C., a man aged 38, who was admitted to the Cook County Psychopathic Hospital on Oct. 15, 1932, had had a chancre fifteen years before, which had been treated with ten injections of arsphenamine. The pupils were of the Argyll Robertson type; the knee jerks were exaggerated, and speech was slurring. The Wassermann reaction of the blood and of the spinal fluid was 4+. The cell count of the spinal fluid was 48; the Pandy test was positive, and the colloidal gold curve was 5555531100. The patient was disoriented for time and place. Retention was poor; calculation was somewhat impaired, and judgment was practically nil. At times the patient was violent, attacking the attendants. At other times he was euphoric and grandiose. For example, he stated that he had $5,000,000 and many yachts and airplanes, and that all this money had been obtained by betting on races.

Fourteen hyperpyrexia treatments were given, the temperature remaining above 103.5 F. for ninety-four hours, and above 105.8 F. for thirty hours. The patient began to improve after the tenth treatment and recovered from all psychotic symptoms by December 18, when he was sent home. Examination of the blood and spinal fluid on December 20 showed: Wassermann reaction of the blood 1+; Wassermann reaction of the spinal fluid, 3+; spinal fluid cell count, 4; Pandy test, positive; colloidal gold curve, 1222100000. Since then the patient has received weekly injections of a bismuth preparation and of tryparsamide. He is at work at his former position, that of salesman.

The treatments were given partly by means of diathermy and partly by means of a hot air cabinet of special construction. In other words, the patient was treated by both external and penetrating heat. Since it is the fever per se which produces these results, it is immaterial what type of machine is used for producing the fever. I have treated patients with diathermy, radiothermy, the electric blanket, hot air cabinets and hot baths and lately with the inductotherm. Each of these methods has some advantages and some disadvantages. Just what apparatus is used depends on the training and inclination of the physician. Like febrile temperatures produce like clinical results in a given patient.

DISCUSSION

DR. PERCIVAL BAILEY: There has recently been developed at the Mayo Clinic a method of creating hyperpyrexia by air conditioning which seems superior to any method heretofore devised.

PROGRESSIVE FACIAL HEMIATROPHY (TWO CASES). DR. LEWIS J. POLLOCK.

F. S., a boy aged 6 years, was born at the seventh month of pregnancy with otherwise normal birth; there was no asphyxia or convulsions. The child was breast fed; he teethed and sat up at 9 months of age, walked at 1 year and talked at 8 months. At the age of 1 year he fell while learning to walk and was "knocked out" for a minute or two. When picked up, he acted as if he were in pain, and the head dropped to the side. When he fell he struck the left side of the head against a chair. Six months later he had a convulsion limited to the right arm and the right side of the face, with loss of consciousness; in a couple of weeks he had another attack, and since then the attacks have continued with increasing severity. During the first few months of 1933 he had about 5 attacks a month.

When examined on May 24, 1933, there was a slight depression over the left frontal bone in which the subcutaneous tissue had atrophied in a circular area, the skin appearing thin and with slightly distended venules. The area is said to have gradually increased in size since it was first noted shortly after the injury.

Fig. 1.—Appearance of F. S.

The following report was submitted on the roentgen examination of the skull: "One's first impression is that the bony differences shown are not as pronounced as the differences obtained on external inspection. This is partly answered by the view made tangent to the bone. This view under a strong light shows that there is considerable difference in the thickness of soft tissues on the outside of the frontal bone so that on the right side the tissues are twice as thick as on the left side. The actual thickness of the bone on the right side is the same as on the left. It can be seen to project outward and a little forward on the right, but the prominence on the right side is partly to be accounted for by the soft tissue difference. The vascular structures look similar on the two sides. The right antrum shows opacity of moderate grade."

There was no other objective evidence of organic neurologic disease. The Wassermann reaction of the blood was negative. There was mild secondary anemia. The urine was normal, and no visceral disease was found.

The boy was treated with sodium bromide, solution of potassium arsenite and an infusion of Adonis vernalis sufficient to keep the blood bromine at 150 mg. per hundred cubic centimeters, with cessation of the epileptiform attacks (fig. 1).

H. O. J., a boy aged 15 years, was born normally at full term. The mother died of puerperal fever seven days afterward. During early childhood he was healthy, robust and normally developed.

In the summer of 1927 he was struck beneath the right jaw with a windmill lever. In the fall of 1928 he was struck over the right side of the forehead with a baseball bat, which inflicted only a minor injury. In the summer of 1928, during sleep, he had an epileptiform seizure. In several days another attack occurred. At this time the right side of the face was flushed, and the right cheek was less prominent than the left. A depression was present over the right temple and the supra-orbital region. The skin felt hard and firmly attached to the subcutaneous tissue. The seizures continued, occurring two or three times a week nocturnally. In 1929, the atrophy had progressed considerably and the seizures occurred during the day as well as at night. In 1932 the seizures were controlled with bromide therapy. At this time the atrophy had progressed to a marked degree, being sharply limited to the right side, affecting the skin, subcutaneous tissue and muscles,

Fig. 2.—Appearance of H. O. J.

which are more easily visualized by the illustration than described (fig. 2). The skin is diffusely pigmented and has become soft. No other objective neurologic signs are present. There is no visceral disease. Despite the marked asymmetry of the two sides of the face, roentgen examinations revealed no change in the bones of the face or the skull.

Comment.—In both of these cases the hemiatrophy was associated with epilepsy. Cases reported in the literature have been found to be associated with many so-called complications, and I believe that of these complications epilepsy is the most frequent. It is a mysterious condition; what produces this peculiar type of trophic disturbance with epilepsy is unknown. The epilepsy is not at all related to the progress of the hemiatrophy. The convulsive seizures are no more frequent or severe during the time the atrophy progresses. It is also of interest that the muscles of the face do not show any change to electrical irritability. Another point is that these patients appear to have marked atrophy of all the soft structures of the face but no atrophy of the bone.

PITUITARY CACHEXIA RESULTING FROM A SUPRASELLAR CYST. DR. LEWIS J. POLLOCK.

E. K., aged 12 years, was brought to the Passavant Memorial Hospital on Oct. 31, 1933, with the complaint of blindness in the left eye of four weeks' duration, headache and vomiting spells of four years' duration and nervousness. She had had a normal birth and development. Tonsillectomy was performed at the age of 2½ years, and she had measles at 3½ years. She started school at the age of 6 years and did well until the fall of 1933. The menses began in May 1933. The family history is of no significance.

The headaches started when the child was 7½ years of age. They were severe and throbbing and lasted for from three to four weeks. At intervals of three or four weeks they would reappear. They were frontal and associated with drowsiness. At first, vomiting occurred before the onset of headache; later it occurred after the headache had been present for some time. The headache and vomiting have continued to the present. In February 1933, drooping of the right eyelid was noted. The left eye was described as being "up and out." There was impaired vision in the left eye. In October 1933, the left eye became blind. Since the age of 6 years, when she weighed 45 pounds (20.4 Kg.), the patient has not gained in weight though she has grown in height.

The patient drank a great deal of water (about a gallon [3,785 cc.] daily). She has been extremely hungry on awakening for the last four or six weeks. The gait was titubating, and she tended to veer toward the right. She walked with the head turned to the left and became fatigued easily. She was continuously somnolent. Occasional enuresis was present one year before admission.

The blood pressure was 90 systolic and 60 diastolic; the pulse rate, 140; the weight, 46 pounds (20.9 Kg.) and the height, 54½ inches (138.4 cm.). Numerous muscular contractions were present over the body. There was an external strabismus of the left eye. The pupils did not react to light or in accommodation. The disks had a white pallor and were sharply outlined. Complete oculomotor paralysis was present on the right side. There was fair vision in the right eye and almost none in the left. There was slight dorsal scoliosis, with the convexity to the left. The abdominal reflexes were brisk; all deep reflexes in the upper extremities were active, except the triceps, which were not elicited; the reflexes of the lower extremities were normal, and there were no pathologic reflexes.

The patient vomited considerably while in the hospital. At one time the blood sugar during fasting was 22.3 mg. per hundred cubic centimeters, and the carbon dioxide-combinng power was only 11 volumes per cent. The urine contained acetone bodies. The patient's condition improved when dextrose was administered intravenously, and the emesis stopped. The intake of fluid was 900 cc., and the output of urine, 465 cc. At another time the intake of fluid was 2,780 cc., and the output of urine, 735 cc. Examination of the blood showed 4,680,000 erythrocytes, 8,500 leukocytes, and 78 per cent hemoglobin; the differential count was normal. The Wassermann and Kahn reactions were negative, and free hydrochloric acid was present in the vomitus. The temperature varied from 98 to 100 F. during the patient's stay in the hospital. The cachexia continued. A roentgenogram revealed a large sella turcica, with evidence of generalized thinning of the posterior and anterior clinoid processes, without any localized erosion. The roentgenologist interpreted this as probably caused by an extrasellar tumor exerting pressure on the sellar contents. Examination of the visual fields revealed no vision in the left eye and a small central field preserved in the right, with vision 20/200. The general condition was too poor to warrant operation at the time.

The patient progressed well until February 26. She had been eating well and gaining in weight. Then she began to vomit again and gradually became sleepy; later she became semicomatose. Vision in the right eye had been failing, and urinary incontinence had developed. The last menstrual period was missed. The pulse rate was 68; the rhythm was irregular, and the blood pressure was 100 systolic and 70 diastolic. The strabismus and optic atrophy were present as at the previous examination. Intravenous injections of dextrose were given for five

days, when the patient became able to take food in small quantities by mouth. A temperature of 99 F. was the highest reached. There were several attacks of generalized shaking, like "chills." The blood sugar was 78 mg. per hundred cubic centimeters.

At the last examination, two months later, the patient was reported as doing well, with no vomiting and few headaches. She had gained 1 pound (0.5 Kg.) in weight. It was hoped that the physical condition could be improved to the point where she could withstand an intracranial operation.

Comment.—There are two interesting features in this case in addition to the attacks. Apparently a rapid lowering of metabolism occurred, with marked somnolence, merging into stupor, a slow pulse rate and hypothermia. With this there was sudden lowering of the blood sugar. I think that on one occasion it was 21 mg. At the same time there was marked reduction in carbon dioxide-combining power, to 14 volumes per cent. I think that there is only one other case on record in which there was so low a carbon dioxide-combining power in the blood and the patient did not die. It is interesting to speculate on the cause of this change.

DISCUSSION

DR. R. P. MACKAY: Has any replacement therapy been instituted?

DR. LEWIS J. POLLOCK: While in the hospital many kinds of anterior lobe pituitary substances were administered. The patient has spontaneously recovered from the attacks and has also recovered while taking anterior lobe pituitary products, so she probably would have recovered spontaneously. She usually responded in about four days.

DR. PERCIVAL BAILEY: When such patients pass into this cachectic condition the basal metabolic rate is very low. It is often thought to be due to hypothyroidism, but many other things can cause this lowering of metabolism. Certainly it is not entirely due to the thyroid in these cases. There is no pituitary preparation on the market which is potent and can safely be given. My colleagues and I are trying to treat such patients with phyrone, but to date the patient has only been made extremely ill by the extract. I suppose one might try extract of the suprarenal cortex. The lowering of the metabolism is a distressing complication of these cases, against which one is practically helpless.

DR. DAVID A. CLEVELAND: For several years I have tried to remove the pineal gland from kittens, using the Horsley-Clark apparatus; my animals all died, frequently at the end of about two weeks, going into a convulsive state before death. After two or three months of such experience I studied the blood sugar and found that death ensued from hypoglycemia. There was often an unmeasurable amount of blood sugar, but usually from 30 to 40 mg. Stimulated by the work of Houssay on the association of the pituitary gland and the pancreas, work has been carried out in almost every laboratory throughout the country, and much is being learned about the relation between the pituitary and other glands, particularly the pancreas. I think that these cases deserve intensive clinical study, and if possible later postmortem study, from that standpoint.

PROGRESSIVE MUSCULAR ATROPHY (SCAPULOHUMERAL TYPE OF VULPIAN AND BERNHARDT). DR. GEORGE B. HASSIN.

A Polish laborer, aged 57, who gave a history of drinking 1½ pints (700 cc.) of alcohol daily since 1918, for five years had had complete paralysis of both upper extremities. He also complained of "cramps" in the muscles of the lower extremities, especially the left biceps muscle. The paralyzed extremities were immobile, hanging loosely by the sides of the chest, and could not be moved in any direction. The muscles involved—the deltoid, supraspinatus, infraspinatus, biceps and triceps—exhibited considerable wasting and only a partial reaction of degeneration. The muscles of the hands—the thenar, hypothenar and interosseal—were much less affected. The tendon reflexes were absent in the upper extremities

and present in the lower, without a Babinski, Rossolimo or similar sign. The cranial nerves, the mentality, the sensibility and the genito-urinary organs were normal. Serologic and genito-urinary studies and chemical analysis of the blood gave negative results.

Biopsy on some atrophied muscles revealed no inflammatory or proliferative changes in the connective tissue; some fibers were reduced in size, but they had preserved their striations—a not uncommon occurrence in cases of spinal amyotrophy.

DISCUSSION

DR. D. M. OLKON: The puzzling feature in this case is the violent muscular cramps in the lower limbs. They have been so severe that on one occasion morphine had to be given hypodermically to relieve the pain and spasm. Another outstanding feature was the low blood sugar, which on repeated examinations was below 80 mg. per hundred cubic centimeters. Even when 16 units of insulin per day, in divided doses, was given, the sugar did not register above 84 mg. The blood and spinal fluid were negative for syphilis, and there were no other abnormalities in either the blood or the spinal fluid to make one think of infection.

There were no clinical signs of compression of the spinal cord or injury to the peripheral nerve.

DR. R. P. MACKAY: Dr. Hall and I have been interested in cases of spinal muscular atrophy due to syphilis. In a clinical study of such patients we have been struck by the frequency with which the atrophy is associated with pain. This pain, it appears, is due to irritation of the dorsal roots of the spinal cord by the syphilitic inflammatory process. I understand that in this patient there is no serologic or other evidence of syphilis. However, this is not sufficient to exclude syphilis as a possible cause, since it appears that many patients with syphilitic spinal muscular atrophy present entirely negative serologic findings, just as happens in many patients with tabes dorsalis.

EPICONUS LESION (?). Presented by DR. D. M. OLKON for DR. GEORGE B. HASSIN.

A French woman, aged 46, whose feet had been frozen six years previously, had had difficulty in walking for nine months because of paralysis of both feet. The paralysis developed suddenly, first in "the left ankle joint" and six months later in the right. It was not possible to determine whether the paralysis had any connection with falls which the patient sustained repeatedly. There was no pain, but paresthesias—a feeling of hot and cold—were often complained of.

Examination revealed: slightly cyanotic feet, which dropped markedly; lively tendon reflexes throughout, normal sensibility and coordination and normal genito-urinary organs, cranial nerves, ocular fundi and visual fields. There was a distinct steppage gait. No atrophy was in evidence, and both faradic and galvanic currents elicited good responses from the extensor hallucis longus and peroneal muscles. The rest of the muscles did not respond to the faradic current, but they responded to a strong galvanic current without changes in the electric formula (the cathodal closure contraction was greater than the anodal closure contraction). Roentgen examination and examination of the spinal fluid gave negative results. Against a diagnosis of epiconus lesion in this case are the onset and course of the paralysis and the presence of the achilles tendon reflexes. However, the history was not altogether reliable; as to the achilles tendon reflexes, their presence in epiconus lesions has been described before.

Comment.—The diagnosis presented here was "epiconus lesion." The clinical findings, however, make such a diagnosis presumptive, without apparent rationale.

DISCUSSION

DR. PETER BASSOE: If there is nothing but the foot-drop, the patient should be able to walk.

DR. D. M. OLKON: She can drag herself along but has to be helped. She can hardly walk at all alone.

A Left Cerebellopontile Angle Syndrome (Multiple Sclerosis?). Dr. Theodore T. Stone.

Miss W. T., white, aged 29, was in good health until May 1932, when she had vertigo, nausea and vomiting. In May 1933, after walking all day, she became dizzy (objective vertigo) and vomited and had a tendency to fall to the left. Turning the head to the left or lying on the left side in bed increased the dizziness and produced retching and vomiting. Tinnitus in the left ear developed two days later and was followed by impaired hearing in the left ear. Blurring of vision occurred at this time to the degree that she could distinguish only moving forms and between light and dark. At this time she experienced paresthesias in the left upper and lower extremity and ataxia and clumsiness in the left hand. There then developed numbness in the left side of the face.

Neurologic examination showed the following objective findings: The head was tilted to the right; there was spontaneous horizontal nystagmus, and on fixation of the eyes to the left the right palpebral fissure was greater than the left. There were weakness of the left external rectus muscle and inability to raise both eyeballs upward. Both pupils dilated and reacted sluggishly to light; accommodation was normal. There were atrophy (primary) of the left optic fundus; temporal pallor of the right optic fundus; hyperesthesia of the left cheek and upper lip; diminished hearing in the left ear, and inability to move the left angle of the mouth as well as the right. The left nasolabial fold was less prominent than the right. There was hemiataxia on the left side, and the abdominal reflexes were present. All deep reflexes were bilaterally brisk. No other neurologic signs were present.

A roentgenogram of the skull showed no abnormalities. The blood count revealed 4,200,000 erythrocytes, 8,100 leukocytes and 70 per cent hemoglobin. The urine was normal. Spinal puncture revealed clear fluid under a pressure of 10 cm. of water. There was no block. The Lange and the Wassermann tests were negative. There were no cells or globulin. The responses to the vestibular tests were within normal limits, and the cochlear tests showed impairment of hearing in the left ear.

A diagnosis of left cerebellopontile angle syndrome (multiple sclerosis?) was made. A tumor of the cerebellopontile angle and arachnoiditis of the posterior fossa were considered, but the course and markedly favorable progress militated against them.

Absolute rest in bed, forcing of fluids and administration of quinine hydrochloride were prescribed. On June 20, 1933, the left hemiataxia, falling to the left, deafness in the left ear and numbness over the left side of the face had disappeared. On July 10, vision had improved, and the patient was able to see and recognize the interns and nurses. She left the hospital on July 11. On August 2 she returned to the hospital because two days previously she had suddenly lost vision completely in both eyes. Examination revealed slight elevation of the disk of the right eye with blurred edges and small hemorrhage about the area of the disk, and practically a flat disk in the left eye with blurred margin and dilated blood vessels (diagnosed as papillitis). One hundred cubic centimeters of 50 per cent dextrose was given on two occasions, and on August 10 an intravenous injection of typhoid vaccine was given. Six injections were given, with a reaction in each instance. After the third injection vision returned and has improved progressively since. The patient now has bilateral atrophy of the optic nerve but is able to come to town alone. She reads and takes care of herself.

DISCUSSION

Dr. Lewis J. Pollock: It is of interest relative to the symptomatology and possible localization that there have been symptoms referable to the brain stem similar to those that occur in lesions of the cerebellopontile angle. There was no evidence of increased intracranial tension, and there then appeared to be a remission.

Dr. Peter Bassoe: The case is extremely interesting to me on account of the fluctuation of vision and the eyegrounds. The condition evidently belongs to

the obscure borderland of multiple sclerosis. Hassin and I reported such a case with the title "Multiple Degenerative Softening." Dr. Patrick and I saw in Milwaukee a striking case with a remarkably fluctuating course. At one time the disks appeared completely atrophied and there was no vision, but it came back and later disappeared. I hesitate to call the condition multiple sclerosis, but I think it is related to it.

PSEUDOBULBAR PARALYSIS WITH A CEREBELLAR SYNDROME IN A FIVE YEAR OLD CHILD. DR. R. P. MACKAY.

M. A. G., a girl aged 5 years, came to the neurologic outpatient department of St. Luke's Hospital on April 30, 1934. The father at the time had pulmonary tuberculosis and was a patient in the Chicago Municipal Tuberculosis Sanitarium; the mother was in good physical health; there were no children except the patient.

The patient was born without difficulty at full term. She was artificially fed and received cod liver oil and orange juice in the usual way. She appeared normal in every respect until 1 year of age, when she learned to walk only on her toes; she was unable to bring the heels down on the floor. When she learned to talk (also at 1 year of age), speech was not distinct. The normal drooling of infancy did not disappear but has persisted to the present time. She eventually learned to walk fairly well and to speak and even to sing, but she always tended to stub her toes on the pavement and never could run as well as other children. She often fell while playing. About fourteen months prior to examination she had a cough with fever and diarrhea, an illness which lasted two weeks and from which she recovered completely, without neurologic complications. She has never suffered from any of the exanthems, diphtheria or other infectious disease.

One month prior to admission she began within a few days to stagger in gait; speech became progressively more dysarthric, and she choked in eating and drinking. The drooling which had been present since infancy rapidly became much worse. She was eventually scarcely able to walk because of stiffness and unsteadiness of the legs; her speech could be understood by no one except her parents, and feeding became a problem because of the constant choking.

General physical examination gave negative results. The rectal temperature was 99 F.; the pulse rate, 90, and the respiratory rate, 20. Neurologic examination on May 1 revealed normal pupils and optic fundi. The perimetric fields were normal to rough testing. There was moderate lateral nystagmus, more marked to the right. There was no extra-ocular paralysis. The lower jaw hung open constantly and could be closed voluntarily only with difficulty. There was bilateral voluntary facial weakness, almost complete on the right with, however, little or no weakness in laughing or crying. Drooling of saliva was constant. Palatal elevation was extremely weak; there were marked dysarthria and a nasal quality in the speech, but phonation was relatively good. The tongue protruded to the right. There was no atrophy of the cranial muscles. Both arms were slightly weak, especially in the muscles of the shoulders, with slight scapular winging. Both legs were moderately weak and spastic; there were no fibrillations or atrophy. The tendon reflexes were all hyperactive, but equal on the two sides of the body; the abdominal reflexes were absent, and the Babinski sign was strongly positive on both sides. There was no abnormality of sensation in any part of the body.

Cerebellar tests revealed a moderate degree of dysmetria in all extremities, with severe adiadokokinesis, a marked "cerebellar rebound phenomenon" in both arms, a strongly positive Romberg sign and an extremely ataxic and spastic gait whether the eyes were open or closed.

Urinalysis gave negative results; the red blood cells numbered 3,950,000; there was 16.15 Gm. of hemoglobin per hundred cubic centimeters (76 per cent), and the leukocytes numbered 11,400, of which 50 per cent were neutrophilic polymorphonuclears and 41 per cent lymphocytes, with 7 per cent monocytes, 1 per cent eosinophils and 1 per cent basophil cells. The Mantoux test was negative. Cultures from the nose and throat were negative for the bacillus of diphtheria, and vaginal smears showed no gonococci. Spinal puncture revealed a clear, colorless fluid under

normal pressure. There was a prompt response to jugular compression. The Ross-Jones and Pandy tests for globulin were negative; no cells were found; both the Kahn and the Wassermann test were negative, and the colloidal gold reaction was 0000000000. The total protein in the spinal fluid was 15 mg. per hundred cubic centimeters. Roentgen examination of the skull revealed nothing abnormal.

In summary, the patient presented bilateral involvement of the pyramidal tract, predominantly affecting the bulbar apparatus but also producing definite spasticity in the legs, together with a marked cerebellar syndrome. The best descriptive diagnosis seemed to be pseudobulbar palsy with cerebellar ataxia.

Anatomically, it seemed possible to explain all the symptoms by a pontile or pontobulbar lesion, but difficulty was encountered in postulating the nature of the lesion. The patient had had some difficulty in walking and speaking and some drooling since the age of 1 year, followed by an acute exacerbation within the past month. A neoplastic lesion seemed unlikely because of the selectively motor type of disability, with absence of all sensory involvement, the absence of all signs of increased intracranial pressure and the peculiar history. A vascular lesion also seemed unlikely, largely from the selective nature of the disease process, the absence of other evidences of vascular disease and again the history. It seemed most reasonable to attribute the condition to selective abiotrophy and degeneration of the pyramidal and cerebellar apparatus, although the possibility of an encephalitic process could not be rigidly excluded.

DISCUSSION

DR. PETER BASSOE: This is a remarkable case; there is the entire picture of pseudobulbar palsy, except the spontaneous laughing and weeping of adults; but in addition there is also a cerebellar syndrome. The child staggers like a patient with cerebellar ataxia, which makes me suspect that, considering the rarity of any kind of encephalitic process in children, one might think of a tumor in the cerebellum, perhaps an astrocytoma.

DR. PERCIVAL BAILEY: Children rarely have progressive chronic polioencephalitis. Whenever I see a case of this sort it usually turns out to be an instance of diffuse tumor of the brain stem, what the pediatrician used to call hypertrophy of the pons. I think this condition should be considered rather than encephalitis or an inflammatory lesion of any kind.

DR. R. P. MACKAY: Do these children show symptoms referable to the lower motor region also?

DR. PERCIVAL BAILEY: Yes, and they often die before they show any evidence of increased intracranial tension. It is for this reason that the diagnosis is not made.

DR. R. P. MACKAY: If encephalitis is so rare in children, what should one say about the cases of cerebral spastic paralysis of childhood, developing perhaps years after birth, which are seen in so many hospitals for crippled children? They certainly cannot all be due to tumors. Are they all abiotrophic, or are some of them encephalitic in origin?

DR. PETER BASSOE: I understood Dr. Bailey to say that he does not believe in a chronic progressive encephalitis in children but that he does not deny the existence of an acute type. I have seen an anatomically verified case of epidemic encephalitis in a child aged 4 weeks.

DR. LEWIS J. POLLOCK: The point of interest to me is that it seems that there is a disproportion of weakness in the face and tongue as compared with the extremities; it did not seem to me that there was the same type of weakness as is seen in cases of pseudobulbar palsy due to bilateral cerebral lesions. I agree that the condition is pseudobulbar palsy in that the bulbar muscles are involved without evidence of involvement of the motor cells of the cranial nerves. It would be interesting, I think, to see what the electrical reaction would show. Is there a myasthenic reaction in these muscles? The child could not bite my finger so that I could feel any pressure, and after 6 or 7 bites she could hardly make any movement.

MENINGIOMA OF THE SPHENOID RIDGE. DR. PERCIVAL BAILEY.

In 1931, the patient noticed a swelling in the left supra-orbital region which did not increase in size and was not tender or painful. About the same time exophthalmos developed on the left side. Six months before examination the patient had severe headaches for four days. Except for these symptoms he has been free from complaints.

Examination disclosed, in the left temporal region about 7 cm. above and posterior to the left supra-orbital ridge, a flat protrusion of the bone, from 4 to 5 cm. in diameter. The swelling was not tender. Its surface was hard and did not fluctuate. The skin over it was freely movable; the mass did not pulsate, and no bruit was heard. Examination of the eyes disclosed visual acuity in the right eye of 10/10 and in the left of 8/10. The exophthalmometer showed the following degree of exophthalmos: right eye, 19 mm.; left eye, 25 mm. The left palpebral fissure was widened. Inside the orbit one could feel near the supra-orbital margin a mass about the size of a hazelnut which arose from the roof of the orbit. The pupils, fundi and visual fields were normal. Examination otherwise gave negative results.

Roentgen examination revealed the left sphenoid ridge to be thickened and increased in density. The pathologic process extended into the roof of the orbit, including the orbital fissure and the anterior part of the temporal bone. Seemingly the middle meningeal artery ran through the center of the mass.

Craniotomy was done by me on May 28, 1932. The overlying bone was roughened and protruded and was attached to the dura. When the skull was trephined the bone bled profusely. The bone broke above the exostosis in a curved line almost parallel to the upper margin of the bone flap. The bone was then cautiously rongeured away, the outer wall of the orbital roof as well as nearly the entire lateral orbital wall, the anterior part of the temporal bone and most of the sphenoid bone, especially the sphenoid ridge being removed. The dura was everywhere closely adherent to the bone.

The tumor was removed en bloc by Dr. Paul C. Bucy at a second operation. The dura over the temporal lobe was opened, and the incision extended into the middle fossa. Here the dura was thickened. It was apparent that this thickening represented the base of the tumor.

The postoperative course was uneventful, except for permanent paralysis of the left abducens nerve. The exophthalmos receded. There is still a slight exophthalmos on the left; and the patient complains of diplopia.

Comment.—I have been struck by the number of patients one finds with an infiltration of the bone around the basilar regions of the skull. It was formerly taught that meningeal tumors did not invade the base of the skull, and that statement has been made in the literature, but my co-workers and I have found a large number of tumors of this type that have invaded the skull and caused exostosis. We have 2 other cases similar to the case presented here. On operation in such cases we find a small flat meningeal tumor which has invaded the bone. The patients usually come to the hospital because of the exophthalmos long before they have any other symptoms, for the part of the tumor inside the head is very small.

CONGENITAL DERMAL SINUS GIVING RISE TO A SUBDURAL ABSCESS AT THE LEVEL OF THE FOURTH THORACIC VERTEBRA. DR. PERCIVAL BAILEY.

L. I., a girl aged 5 years, since birth had had a small dimple in the midline of the upper portion of the back. In all other respects the child seemed normal. At 6 months of age the site of the dimple became swollen and purple and discharged a slightly bloody material. The patient at this time had high fever and a sore throat. Shortly afterward she began to vomit frequently. A physician noted that the back was rigid, and on lumbar puncture he found 150 cells in the spinal fluid. A pellicle formed in the fluid after it had stood for an hour. A portion of the spinal fluid was injected into a guinea-pig, and the animal died three

weeks later. Examination of the animal is said to have revealed evidence of tuberculosis. Another consultant saw the patient at that time and noted that she was "irritable and cranky." The fontanel was not bulging; there was no strabismus and no Kernig sign, but there was definite rigidity of the neck. The consultant thought that the child was suffering from encephalitis. Subsequently another specimen of spinal fluid was injected into a guinea-pig, and this animal also died. This was considered conclusive proof that the child was suffering from tuberculous meningitis.

The illness, with great irritability, evening fever, vomiting, loss of appetite and rigidity of the back, continued with varying degrees of intensity for about eighteen months, when, for no apparent reason, the child recovered and remained well until November 1932. She was then 5 years of age. During the intervening three years, however, there had been an occasional discharge from the dimple of a few drops of milky material which was at times blood-stained. This occurred two or three times a year, and on two occasions the skin surrounding the dimple became red and swollen.

During the latter part of November 1932 the patient began to complain of pain in the neck and back, particularly at night. She was taken to the Children's Memorial Hospital, where it was observed that she constantly rubbed both hands and arms, apparently because of localized discomfort. Because of this constant rubbing the skin over these areas was inflamed and excoriated. There were spasm of the sternocleidomastoid muscle, scoliosis of the upper thoracic vertebrae with the convexity to the right and a small, slightly elevated dimple just above the spine of the fifth thoracic vertebra. Both knee and ankle jerks were lively, and sustained ankle clonus was present bilaterally. The right plantar reflex was of the extensor type, and the left of the flexor type. Roentgenograms showed an incomplete fusion of the laminae of the fourth thoracic vertebra and a marked spinal curvature. After ten days in the hospital the patient's condition improved greatly, and she was sent home. During the following months the gait became progressively more spastic, and the reflexes of the lower extremities more active, and at times local tenderness was present over the fourth and fifth thoracic vertebrae. On April 22, 1933, lumbar puncture yielded a clear fluid, under normal pressure, containing 3 lymphocytes and giving a negative reaction for globulin (Pandy); the Wassermann test was negative. Late in June the patient began to scratch and rub the ulnar surfaces of both hands and arms, presumably as a result of paresthesias. It was noted on July 3 that as a result of the rubbing the ulnar surfaces of both forearms were red and inflamed. The findings on neurologic examination at that time were essentially as they had been previously. Roentgenograms showed no change in the appearance of the thoracic vertebrae or of the defect in the fourth vertebra. A lumbar puncture revealed xanthochromic fluid under very low pressure, which contained 50 red blood corpuscles and an increased quantity of globulin as tested by Pandy's method. Queckenstedt's test revealed a partial block in the spinal subarachnoid space.

On July 18 the patient was admitted to the Bobs Roberts Hospital of the University of Chicago Clinics for an exploratory laminectomy. However, measles developed shortly after, thus delaying an operation. On August 10 examination revealed the dimple previously noted just above the spine of the fifth thoracic vertebra. This was not tender and seemed freely movable on the underlying tissue, but no discharge could be expressed from it. Neurologic examination revealed no abnormality of any of the cranial nerves. The tendon reflexes of the upper extremities were normal; those of the lower were lively, the right somewhat more so than the left. Sustained ankle clonus was present on the right; abortive clonus was obtained on the left. The right abdominal reflexes were sluggish, and the left, brisk. Both plantar reflexes were extensor in type. No definite sensory level was found, although at times one gained the impression that sensory perception was not as acute over the portion of the body below the upper thoracic region. The finer modalities of sensation (two point discrimination, position sense, stereognosis, etc.) could not be tested owing to the patient's failure to cooperate. There

was no localized atrophy in any muscle group, but in general the strength was poor. No increased resistance was encountered on passive movement of the upper extremities, but there was definite extensor rigidity in the lower extremities. This was more marked on the right. Muscular coordination was fairly good throughout. Scoliosis with its convexity to the right in the upper thoracic region and a compensatory curve in the lower thoracic and the upper lumbar region were present. The gait was spastic; the patient walked with small, uncertain steps. When standing with the feet together and the eyes open she did not sway, but on closing the eyes she tended to fall to one or the other side.

Lumbar puncture at this time showed clear cerebrospinal fluid under a pressure of 110 mm. of fluid. Jugular compression (bilateral) caused a slow rise to 240 mm. and an equally slow return to 110 mm. after release of the pressure, indicating a partial block in the subarachnoid space. Removal of 3 cc. of fluid caused the pressure to fall to 80 mm. No cells were found in the fluid, and the total protein content was 64 mg. Roentgenograms revealed the defective closure of the laminae of the fourth thoracic vertebra previously mentioned.

On August 16, with the patient under ether anesthesia, the third, fourth and fifth thoracic laminae were removed. The spine of the fourth thoracic vertebra was absent, and the imperfect closure of the posterior neural arch, which had been observed in the roentgenograms, was seen. The dimple was continuous with a tough stalk of tissue, about 3 mm. in diameter, which contained a minute central canal from which a thick caseous material could be expressed. The stalk extended from the dimple downward through the posterior spinal muscles, through the defect in the laminae of the fourth thoracic vertebra to the dura mater, to which it was firmly attached. Beneath the dura mater at this point a firm mass was palpable. The dura mater above the tumor mass pulsated normally, but no pulsation was present below it. The dura mater was incised around the fibrous mass, exposing a thickened, white, opaque arachnoid membrane. The arachnoid about the margins of the tumor fused with the greatly thickened dura, and both were incorporated in the thick fibrous mass which was firmly adherent to the posterior surface of the spinal cord. This mass could be removed only by cutting it off the posterior surface of the spinal cord. This procedure revealed within the mass numerous cystic spaces containing a thick caseous material, which on examination was found to contain many pus cells but was sterile on culture. After removal of the fibrous mass, the entire spinal cord felt exceedingly firm at this level for a distance of from 1.5 to 2 cm. Laterally the spinal cord was firmly adherent to the much thickened arachnoid and dura mater, but no additional masses or abscesses were found. The dura mater was closed above the site from which the tumor had been removed, but closure at that point was not possible because of the large dural defect. The remaining closure was made in the usual manner except that a small soft rubber drain was left in place.

The postoperative course was surprisingly calm. Except for a moderate amount of pain at the site of operation the patient had no complaints. Both sensation and movement in the lower extremities remained good. Since the cultures of the purulent material were sterile the drain was removed on the second day and the wound healed per primam. For the first week there was urinary and fecal incontinence, but then complete control of the bowel was restored and partial control of urination, which subsequently became normal.

Neurologic examination two weeks after operation showed little change from the findings on admission. A suggestive level of impairment of perception of pinprick was present at the third thoracic dermatome, but it was by no means definite. The reflexes of the lower extremities were still lively, with ankle and patellar clonus and bilateral plantar responses of the extensor type. The strength in the lower extremities was fairly good, although at first the patient walked on a wide base with a spastic gait. In Romberg's position she was fairly steady, even with the eyes closed.

She was discharged to a convalescent home, and when seen six weeks after operation she had no subjective complaints. She walked well and seemed normal.

Comment.—My associates and I have had 3 such cases in which a small dimple in the back discharged a little pus; at times the patients had symptoms that resembled tuberculous meningitis. Paraplegia developed in all. An operation was performed in each case and a dermal sinus which extended down into the spinal canal was found. After the sinus was removed the patient recovered completely. The presence of a little dimple on the outside which discharges from time to time should indicate the nature of the lesion.

DISCUSSION

DR. LEWIS J. POLLOCK: Perhaps many of the cases that have been reported as instances of spina bifida occulta cervicalis have been cases of congenital dermal sinus. I recall a case in which there was roentgenographic evidence of spina bifida occulta in the cervical region and the overlying skin had a dimple, but it had never discharged.

MYASTHENIA GRAVIS. DR. LEWIS J. POLLOCK.

CASE 1.—S. L., a woman aged 29, has been married for five years and has one living and healthy child. There is no history of any serious organic illness in her family. She has had scarlet fever, whooping cough and measles and she was operated on for appendicitis. Tonsillectomy was performed fifteen years ago. Six months before examination in February 1934 she experienced a "terrific" headache which lasted for thirty minutes, during which she noticed diplopia. Six weeks before examination she was "run down" and consulted a physician.

On Feb. 4, 1934, on arising, she noted difficulty in chewing and manipulating food with the tongue, which seemed to twist about. She swallowed liquids with great difficulty, and some would be regurgitated through the nose. Speech was affected, and she could not clear her throat. The condition grew worse, the tongue seeming to grow larger; swallowing, talking, kissing and sucking became difficult and defective. She tired easily, particularly in the late part of the day.

When she was seen on March 13, the disabilities mentioned were present. Repeated closure and opening of the lids produced rapid fatigue in the levator palpebrae muscles. The patient could not whistle, pucker her lips or show her teeth. There was dysphagia for liquids and solids. A nasal type of speech was present. There was weakness in both external rectus muscles. The muscles of the extremities were feeble and tired easily. The deep reflexes were diminished. The superficial reflexes were conserved. There was no objective sensory loss. Direct myotatic irritability was increased, and a myasthenic reaction was present in the muscles of the face.

At first 5 and later 15 Gm. of glycine was given daily, and ¼ grain (0.016 Gm.) of ephedrine three times a day. On May 5, considerable improvement was seen, the patient was able to kiss, suck, talk and drink much better, she became fatigued less readily, and no weakness of the extra-ocular muscles was found. The tongue moved more readily, and she could swallow a bolus of food readily.

CASE 2.—Mrs. J. N. S., who had been seen by Dr. Patrick in March 1922, when she was 47, was married and had had one child, following whose birth she had had eclampsia. In December 1921, after some irregularity of menstruation, amenorrhea ensued. She had had sick headaches since the age of 30, and for thirteen years sharp darting pains from the right eyebrow over the scalp. In February 1922 blurring of vision, diplopia and tubular vision were noted. The eyes tired easily, and for three weeks there was ptosis of the left eyelid and for two days ptosis of the right eyelid. The patient complained that the whole body felt as if it were swollen to twice its normal size. She had always had absence of sweating over the left side of the face. She showed great fatigue of the levator palpebrae and of the ocular muscles. General fatigue was present, and she was readily exhausted. There was no dysphagia or weakness in the masseter muscles. Under treatment with rest and strychnine the condition improved, and in September 1922 there were less fatigue and ptosis. General fatigue remained the same. The

patient complained of a sense of heaviness and a sense of constriction below the knees and the toes. She took strychnine for three years, with great improvement, followed by a remission.

She was seen again on Oct. 9, 1933. For several years she had experienced attacks of weakness so severe that she felt as if she were going to die; usually they occurred at night. Lately the left eyelid had begun to droop and then the right. For three weeks she had had difficulty in swallowing and chewing. She had had pyuria in 1930, and secondary anemia. She had at times had attacks of vertigo lasting thirty seconds. When she was seen there were ptosis of the right lid, some dysarthria and dysphagia, particularly with solids. She became fatigued readily and was tired most of the time. Chewing was difficult, and the masseter muscles tired quickly. She had great difficulty in clearing her throat of mucus.

Fifteen grams of glycine was given daily, with ephedrine and strychnine.

The ptosis has now disappeared; there is no dysarthria or dysphagia. The patient's general strength is good, and a remission has been brought about.

Case 3.—H. E. A. was seen in February 1921, when he entered the Wesley Memorial Hospital complaining of weakness and drooping of the right lower eyelid. He was then 46 and had been married for twenty-two years. His wife had had four miscarriages and had two living children. He had had measles, mumps, malaria, whooping cough, influenza, amebic dysentery and gonorrhea. The family history was essentially unimportant. On January 2, he became ill with what he thought was a "cold." During the preceding week he had been unable to sleep. When he went to work he was very weak and unable to work; that night he was again unable to sleep, and on the following day he was so weak that he was unable to stand for any length of time. On the next day he could not elevate the right upper eyelid. Since then the weakness had progressively increased. The weakness was generalized, affecting the arms so that he could not rest his head on his hands or grasp objects tightly. When he elevated the right eyelid with his finger the light hurt his eye, and he was unable to see distant objects. At times the eye burned as if it had "tobacco juice" in it.

Bilateral ptosis of the lids was found; it was more marked on the right. The right pupil was larger than the left, and the reflex response to light was sluggish. There was slight horizontal nystagmus in both eyes on looking laterally and counterclockwise nystagmus on looking to the left. There was a slight convergent strabismus. There was marked weakness in the masseter muscles, which increased with succeeding movements. After repeatedly opening and closing the left eyelid, the upper lid could not be elevated. There was difficulty in swallowing solid food. There was generalized weakness of the extremities with great fatigability. The fundi were normal. No sensory loss was found. The achilles tendon jerks were diminished; otherwise the reflexes were normal. There was no persistent thymus gland.

The urine was normal. There was mild secondary anemia, and the basal metabolic rate was —15. Examination of the spinal fluid revealed no abnormalities, and the Wassermann reaction of the blood was negative. Occasionally a slight elevation of temperature was noted; the pulse was usually rapid, but at times slower, showing variations from 120 to 68 in the same day. The blood pressure was 110 systolic and 60 diastolic.

A diagnosis of myasthenia gravis was made, and it was thought that the acute attack beginning with insomnia might possibly have been epidemic encephalitis.

The patient apparently recovered from the myasthenia. He returned on Oct. 8, 1931, when for three months he had noticed a tremor of the left arm. The left upper extremity was rigid, and movements were slow. There was coarse tremor in the extremity invoked by voluntary movements, but it was not a typical intention tremor. The gait was that of parkinsonism. The facies was slightly immobile, and mild sialorrhea was present. The right pupil was larger than the left; neither reacted to light. The blood pressure was 120 systolic 80 diastolic. No visceral disease was found. It was considered that the condition was a sequel of epidemic encephalitis.

CASE 4.—D. C. B., aged 68, a minister, the history of whose birth is normal, was a healthy child until the age of 10, when he began to have severe nightmares which persisted for four years. Each winter he had an attack of bronchitis. In 1915, the appendix and part of the omentum were removed. From 1915 to 1919 he enjoyed perfect health. In 1923 he had an attack of pleurisy, from which he recovered. About March 1926 he had some form of infection, with high fever, and at this time had diplopia and drooping of the left eyelid. The diplopia gradually disappeared, but the drooping of the lid persisted, disappearing for only a few minutes after awakening. In June 1926, the voice became guttural, and he had difficulty in speaking. After a rest of a few days he could again phonate for a few minutes. He was compelled to give up public speaking. There then developed difficulty in chewing and swallowing, and he noticed weakness in the arms. The condition was diagnosed as myasthenia gravis, and he was treated with strychnine, with some improvement.

During a course of physical therapy in Germany, from June to September 1927, he improved. From 1927 to 1933 he was unable to preach; he had dysphagia and dysarthria and was unable to move his lips adequately or to hold his eyelids open. He was able to phonate for only a few minutes. In June 1933, after a few months of treatment with 15 Gm. of glycine daily, there was improvement in swallowing, speaking and the use of the tongue and lips, but the drooping of the lids remained unchanged. In February 1934 the patient had improved to such a degree that he was able to preach for over an hour, and he has retained this increase of function until the present time.

Comment.—In 1 fatal case, the muscles affected were those not often affected in cases of myasthenia gravis. Instead of bilateral ptosis the patient was unable to close the eyes and had weakness of all facial muscles in addition to the muscles of the extremities. I have observed that in this type of case remissions do not occur, and there are fatigability and weakness that are constant and not developed merely by activity. I have thought that this group lies somewhere between myasthenia gravis and muscular dystrophy. The muscle tissue showed little evidence of lymphorrhagia. Striated muscle fibers adjacent to normal ones could not be demonstrated.

DISCUSSION

DR. VICTOR E. GONDA: A patient was seen by Dr. Bassoe and me several years ago who had symptoms, including the myasthenic electrical reaction, typical of myasthenia gravis. Tryparsamide was administered as a tonic; after two series of treatments the patient recovered. Now, seven years later, she is well and doing hard work, seemingly without the slightest signs of myasthenia.

DR. PETER BASSOE: The patient whose case was described by Dr. Gonda was seen last week, and she said that she had had no trouble for seven years. She had had marked ptosis, for which an operation had been suggested. The symptoms were typical. Such a long intermission in this disease is rare, but to my mind it may be a pure coincidence and not proof of the curative effect of tryparsamide in this disease.

LID CLOSURE REFLEX. DR. BENJAMIN BOSHES.

Mrs. L. F., aged 42, a housewife, on whom cholecystectomy had been performed fifteen years before, on Dec. 31, 1933, fell on her buttocks and head. She was unconscious and later comatose for several days. When she became conscious, she was unable to protrude the tongue, and the left side of the face felt stiff. She had a headache which was not relieved by spinal puncture. The headaches, which still recur and are of a bursting type, are on the left side. Other residual symptoms were weakness, evanescent paralysis of the left leg and a feeling of formication on the left side of the body. In rising from the sitting position she staggered because of weakness. In April 1934 the right pupil was dilated and failed to react to light. One month later she had a sudden pain in the left side of the chest, radiating toward the spine, and became unconscious; the jaws moved from side to side and the body was stiff. The extremities were cold, and she was drowsy for some time.

On the next day a terrific headache began at the occiput and spread forward. Five hours later vomiting occurred without nausea. Recently the muscles of the face have felt stiff again. Occasionally she feels a trickling sensation inside the skull when she lies down. Lately there has been partial loss of memory for recent events.

Physical examination gave the following results: The blood pressure was 160 systolic and 100 diastolic. The right nasolabial fold was deeper than the left, and the right palpebral fissure was wider. The jaw deviated to the left when the mouth was opened. There was no pastpointing or other motor disturbances. The achilles tendon jerks were absent. The left knee jerk was absent, and the right knee jerk was weakly present. The left ulnar jerk was absent; the right was diminished. The plantar reflexes were diminished. No pathologic reflexes were present. There was slight diminution in vibration sense in the upper extremity. Stocking-like analgesia was present below the left knee. The optic disks were normal. The temperature and pulse were normal. The urine, blood and basal metabolic rate were normal. The Wassermann and Kahn tests of the blood were negative. Spinal puncture yielded a clear, colorless fluid, with an initial pressure of 18 cm. of water; there was no block; there were 4 cells per cubic millimeter; there was no globulin and albumin was not increased; the Wassermann reaction was negative, and the response to the Lange test was 0000000000. A roentgenogram of the skull showed only some calcification of the falx cerebri.

The right pupil was dilated and irregular and did not react to light or in accommodation. The left was small, from 1/16 to 1/8 inch (0.16 to 0.32 cm.), and reacted to light and in accommodation. The left reacted consensually but not the right. Closure of the eyelids caused both pupils to contract to a pinpoint. The reaction was more marked on the right side. (The patient has known of the pupillary changes in the right eye for eight years.)

Special studies of the reaction of the pupils to drugs revealed no change with a 0.2 per cent solution of physostigmine. The right pupil dilated from 7 to 9 mm. with a 1 per cent solution of atropine; then all pupillary reactions disappeared. With a 2 per cent solution of cocaine the right pupil dilated from 7 to 9 mm. in fifteen minutes. The reflex of the lid then disappeared. An epinephrine substitute, a drug with an action resembling that of histamine, caused pain and some "pulling" but no objective change in the pupil. Injection of 2 per cent procaine hydrochloride into the right facial nerve at the stylomastoid foramen caused the reflex of the right lid to disappear as paralysis of the facial musculature, especially the orbicularis oculi muscle, occurred. The reflex was still present on the left, but the closure of the left lid did not affect the right pupil. Movement of the eyeball in all directions produced no change in the pupil. The reflex returned on the right side with return of function of the facial musculature.

Comment.—This patient came to the clinic because of several cerebrovascular accidents with hemiplegia on the right side and motor aphasia. The lid-closing reflex was noted during study. There were no ankle or knee reflexes, and this, coupled with the pupillary changes, led to a diagnosis of tabes dorsalis. Serologic tests have always been negative with both the blood and the spinal fluid. The right pupil does not react to light or in accommodation, but when the patient closes the lids the pupil promptly contracts. This contraction is independent of light or darkness. The left pupil reacts to light and in accommodation, and while it is smaller than the right it still shows the lid closing reflex. The sensory arc of the reflex is apparently in the third and the motor arc in the seventh nerve.

Ependymoma of the Cauda Equina. Dr. Percival Bailey.

A white girl, aged 10 years, somewhat small for her age, was referred to the University of Chicago Clinics from the Children's Memorial Hospital on Jan. 2, 1932. She had had a lump in the back for three or four years; difficulty in walking had been present for about the same length of time and inability to move the left ankle for the past year or two. Four years previously, while playing, the father threw the patient roughly over his shoulder; that evening she woke up crying with pain in the lower part of the head. Since that time she had awakened almost

every night complaining of pain in the back and in the popliteal space. The other symptoms came on insidiously. The lump developed gradually and at the same time the child began to stoop forward in walking. Gradually weakness developed so that the child became unable to support herself. The left leg was considerably more involved than the right, particularly the ankle. The patient lost weight, although her appetite was good.

At the time of admission the patient was emaciated but not acutely ill. General physical examination gave negative results. Neurologically there were kyphosis and scoliosis at the first lumbar vertebra, the scoliosis having its concavity to the left. Movements of the legs were moderately strong at the hip and knee, and there was no weakness of the abdominal muscles. The bladder was distended and could be palpated 8 cm. above the os pubis. The ventral flexor muscles of the trunk were extremely weak. There was little dorsiflexion of the toes or of the ankle on the left side. There was a positive Kernig sign on the left, but not on the right. Both knee and ankle jerks were absent, and plantar stimulation produced a flexor response. There were anesthesia to pinprick and cotton and hypesthesia to cold over the third, fourth and fifth sacral dermatomes and anesthesia to pinprick and cotton over the first and second sacral dermatomes and part of the fifth lumbar dermatome on both sides. There was a small area of hyperesthesia over the left side of the lower part of the dorsal and upper part of the lumbar region of the spine. Roentgenograms revealed concavity of the posterior walls of the bodies of the first to the fifth lumbar vertebra and to a lesser extent of the first sacral vertebra, producing a narrowing in the anteroposterior diameter of the bodies. The spinal canal was grossly dilated in the anteroposterior diameter throughout the lumbar region.

On January 6 the laminae of the vertebrae from the twelfth thoracic to the first sacral were removed. The laminae had been eroded in many places, and the underlying dura was visible through large defects in the bone. The entire bone of the laminae was of paper thinness. When cut through they sprang apart owing to the tension within the dura. The dura was dark and purplish and bled from many points. The incision was extended to the lower margin of the ninth dorsal vertebra, where the dura pulsated. When the dura was incised, a large mass entirely filling the spinal canal, was found. It was adherent to the dura, and in the lower lumbar region there was no line of cleavage between the tumor and the dura. In the upper part of the lumbar and in the dorsal region, however, the dura was easily stripped off the tumor, although with considerable bleeding. Nerve roots were seen arising from the lateral portion of the mass and passing downward and lateral to the base, which occupied the lumbar portion of the canal. The tumor merged imperceptibly with the spinal cord above the level of the twelfth dorsal vertebra, although as the ninth vertebra was approached the spinal cord appeared more normal. The tumor, although of firm consistency, was readily scooped out with a dull pituitary spoon. The entire center of the mass from the twelfth dorsal to the fifth lumbar vertebra was removed in this way. At the close of the operation the patient could move her thighs considerably. The use of a retention catheter was necessary for several days. Convalescence, however, was smooth, and the wound healed by primary intention.

Two weeks after the operation there were a positive Beevor sign and definite weakness of the lower abdominal muscles. The areas of anesthesia were unchanged. The muscles of the thighs were weak; the muscles of the legs were weak, but the patient was able to carry out plantar flexion of the right foot; dorsiflexion on the left was through a moderate range; plantar flexion on the left was much better. The knee and ankle jerks were absent, and the plantar response was still of the flexor type.

A body cast was applied three weeks after operation, and the patient was discharged to a children's hospital on February 3. Before discharge four treatments of 275 roentgens each were administered to the lumbar and sacral regions every other day from January 16 to January 22. A second course of roentgenotherapy was administered from March 12 to 18, and a third course was given between May 27 and June 3.

The neurologic status in June was practically the same as immediately after the operation, except that there was a small ulcer at the end of the fifth left toe.

On Sept. 16, 1932, and March 20, 1933, five roentgen treatments of 275 roentgens each were administered over the same areas of the lower lumbar region as before. Neurologic examination at those times showed little change.

In June 1933 a painless ulcer of the left buttock, about the size of a silver dollar, was present. The trophic lesion rapidly decreased in size and had almost healed by August 1. On April 25, 1934, the patient was able to walk without the aid of a back brace or foot support, although she was unsteady and dragged the left foot. She had anesthesia to pinprick and cotton wool over the five sacral dermatomes on the left and the third, fourth and fifth sacral dermatomes on the right, with complete paralysis of the left tibialis anticus muscle and slight weakness of the dorsiflexor muscles of the toes of the abdominal wall low on the right. The knee and ankle jerks were still absent. The patient was unable to sit up unaided. She had good control of the bowels and bladder. A roentgenogram of the lumbar portion of the spine showed a marked increase in lordosis, but little change otherwise from the roentgenograms taken in January 1932. A series of roentgen treatments was given, the exact dosage of which is not known.

Comment.—The ependymoma is the most common gliomatous tumor in the spinal cord. I wish to emphasize the dilatation of the spinal canal by this tumor. Recently an article in the *Bulletin of the New York Neurological Institute* called attention to the frequency of this alteration. I think that more attention should be paid to the size of the spinal canal. I recently observed a case of tumor at the level of the third cervical vertebra in which the canal was markedly enlarged. The patient was 14 years of age, and the dilatation of the canal was obvious. It is possible that dilatations of the spinal canal will be found more frequently if their occurrence is kept in mind.

DISCUSSION

DR. PETER BASSOE: Dr. Davis will remember the case of a man with a tumor of the cervical portion of the spinal cord in which such a dilatation was marked and was helpful in making the differential diagnosis.

A CASE FOR DIAGNOSIS. DR. PERCIVAL BAILEY.

E. H. L., aged 8 years, was first seen in May 1933. He was admitted to the hospital with a history of lack of concentration and failing ability at school since Christmas 1933 and difficulty in walking for the same period of time. He is an only child. His father is 35 years of age and his mother 32. Neither has had any serious illness, although the father has had some gastric symptoms for about three years. There is no history of any disease of the nervous system in the family of either parent.

The patient was born at term, and delivery was normal. He nursed well and had no convulsions or any other abnormal conditions in infancy; the only illnesses that he has had are measles, whooping cough and chickenpox, all of which were without complications. He went to school at the age of 5, and was regarded as a good scholar. However, in November 1932 it was noticed that he frequently lost his place while reading. Because of this lenses were prescribed. About the same time he was sometimes unable to see objects in front of him, and when walking about at home he frequently fell against tables and chairs. His method of walking became peculiar in that the legs were stiff and he frequently walked on his toes. Speech was sometimes slurred and indistinct. Since the age of 3 years he had had frequent attacks of vomiting with headache and slight fever; these attacks lasted about two days and came on five or ten times a year.

When first seen the boy showed no definite peculiarity and was cooperative. He answered questions intelligently and performed simple commands; although he volunteered remarks, he spoke less than a normal boy of his years. General

systemic examination showed no abnormality, and examination of the blood and urine gave normal results.

Neurologic examination was carried out. The first cranial nerve was not tested. The patient could recognize forms and colors in painted pictures. He could read print, but to do so he held the writing close to his eyes and tended to look at it from the left side. Both fundi were clearcut and showed neither swelling nor atrophy. The vessels were of normal caliber, and the general retina showed no abnormality. Both pupils were centrally placed, irregular in outline and 3 mm. in diameter; both reacted to light, but the reaction was sluggish and through a small range; both reacted consensually, the left more than the right. There was no limitation of external ocular movement in any direction. There were slow nystagmoid jerks in both eyes on looking to the left. The left palpebral fissure was smaller than the right. There was no strabismus, exophthalmos or enophthalmos. The corneal reflexes were brisk and equal. The masseter muscles contracted strongly and symmetrically. The jaw did not deviate when lowered against resistance. There was weakness of the lower left side of the face. Hearing was good in both ears. Weber's test was not made. The palate rose in the middle line. There was no dysphagia. Speech was sometimes indistinct and slurring. The sternocleidomastoid and upper trapezii muscles were strong and contracted symmetrically. The tongue was protruded in the middle line and showed no atrophy, tremor or fibrillation.

The tendon jerks were equal on the two sides; all were + with the exception of the knee jerks, which were + +. There was no clonus. The abdominal reflexes were ± and equal on the two sides. The plantar responses were of the extensor type.

The grasp was only moderate in the hands, and the power of the arms was weak but symmetrical. The patient could sit erect without assistance. The power of the lower limbs was normal. There was hypotonia of the left arm, with falling away when the arms were extended.

The appreciation of cotton wool, pinprick and vibration was everywhere normal.

There were marked incoordination and ataxia in the action of the left arm and left hand and moderate incoordination and ataxia in the action of the right arm and right hand. There was no true rombergism.

The arms did not swing freely, the left not moving at all. There was no falling away to either side; the head was held erect, and there was no ataxia on turning rapidly.

On September 11 the patient was unable to speak sufficiently clearly for any one to understand what he tried to say. There was, however, no change in his intellectual or emotional state, apart from that dependent on his being restricted by his illness, and there was no defect in hearing. No convulsions had been noticed at any time. He was unable to sit or stand or to walk unaided. When in bed, the only abnormality was a permanent flexor contraction of the left arm and of the fingers of the left hand. There were no involuntary athetoid movements at rest, and none was present when voluntary movement was attempted with the right arm or right hand.

When the patient was assisted into a sitting position, there was a torsion movement of the trunk and slow athetoid movements of the arms. The left hand was held near the mouth, with acute flexion of all its parts, the head was turned to the right and the right ear was carried to the right shoulder. When the patient was placed in a standing position there were crossing of the legs, with spasm of the adductor muscles, shortening of the tendo Achillis so that he stood on his toes, flexion of the left arm, partial forward flexion of the trunk and rotation of the head to the right. While in this position, if suddenly unsupported, he closed up in acute flexion of all limbs, with the head touching the knees. When he attempted to walk slow torsion movements of the body appeared, quite apart from the weakness of the limbs.

Both ocular fundi showed a normal disk and a normal macula. There was gross restriction of the visual fields, but the patient had sufficient vision in the central angle to recognize people and large objects. Both pupils were regular in

outline, central and circular; the size was 3 mm. and both reacted briskly to light through a good range. There was no limitation of conjugate movement in any direction except upward, and in that direction there was no movement above the horizontal line. Slow nystagmoid jerks occurred in both eyes on lateral movement. The corneal reflex was diminished on both sides, more on the left than on the right. The masseter muscles contracted weakly on both sides. There was weakness on the lower left side of the face. Hearing was good in both ears. The palate showed slight elevation on phonation. There was no palatal reflex on either side. The pharyngeal reflex was diminished on both sides. There was no regurgitation, but there was difficulty in swallowing and the voice was nasal. There was no localized weakness of either the sternocleidomastoid or the trapezius muscle. The tongue was protruded to the left with no atrophy or fibrillation.

The reflexes had changed in that the supinator and achilles jerks were now + +, and there was ankle clonus on both sides, more sustained on the left. The left abdominal reflexes were less than the right. The plantar reflexes were still of the extensor type.

The left arm was in acute flexion at all joints, with weakness of grasp in the right hand. There was cogwheel rigidity in all four limbs on passive flexion, and a strong spasm of the adductor muscles was present in both legs. No abnormality in the appreciation of pinprick was demonstrated on any part of the body. There were marked ataxia and incoordination in the movements of the right hand. The other limbs could not be tested accurately.

Lumbar puncture was performed, May 19. The initial pressure was 200 mm. of water, with the patient quiet and cooperative and with free respiratory movements. On compression of the left jugular vein the pressure rose to 260 mm., and on compression of the right jugular vein, to 270 mm. The fluid was clear and colorless. After removal of 4 cc. of fluid the pressure was 190 mm. The cell count revealed 3 lymphocytes; the protein was 44.5 mg. The Wassermann reaction was negative.

Roentgenograms of the skull were normal. The optic foramina were normal and symmetrical. An encephalogram after removal of 114 cc. of fluid and introduction of an equal amount of air was normal except for slight generalized dilatation of the lateral and third ventricles.

Comment.—I do not know what the disease is, but I think there may be a diffuse glioma of the brain stem.

DISCUSSION

DR. PETER BASSOE: It seems to me that a glioma of the brain stem is the most probable diagnosis. The only case that I recall that resembles it was that of a child in which I made a diagnosis of encephalitis and necropsy revealed a diffuse glioma of the pons.

DR. R. P. MACKAY: I saw a patient this morning with identically the same clinical status exhibited by the patient of Dr. Bailey, except that he had suffered from this combination of disease of the pyramidal and of the extrapyramidal motor tract for about twelve years. The onset occurred at the age of 17 months, following which the disability was progressive for some years and eventually became almost stationary. This seems to me a rather long duration for a diffuse glioma of the brain stem, and I should rather consider the condition to be a degenerative one.

MEDULLOBLASTOMA. DR. PERCIVAL BAILEY.

J. C., aged 4 years had had headaches, vomiting and progressive inability to walk for four months. Examination revealed a cracked pot sound on percussion of the head; bilateral choked disk; dilated pupils, reacting feebly to light; ataxia of the limbs, especially when walking and sitting, and a bilateral Babinski sign. Some vision was present.

Suboccipital craniectomy disclosed a medulloblastoma in the lower part of vermis.

Deep stupor and hyperthermia were present for three days after the operation, when improvement occurred. Intensive radiation was administered, 27 exposures being given between Nov. 11 and Dec. 29, 1932; marked improvement resulted.

On April 17, 1933, the patient felt well except for pain in the back at times. The decompression was not bulging. He walked on a broad base. Thirteen further irradiations were given between April 26 and May 22.

On June 26 the pain was entirely relieved. Twelve exposures were given between July 12 and 26 and 11 more between October 9 and 25.

On Jan. 1, 1934, the patient was still well, with no symptoms of recurrence.

On March 23 he complained of pains over the sacrum, which were not relieved by medication. Tingling sensations were present in the legs, and he had some trouble in urinating. He was bright mentally. He walked well on a slightly broad base.

A further course of roentgen therapy was given between April 6 and 17. Today (May 19) the pains are relieved and the patient feels well. There is probably a recurrence of the tumor in spite of the intensive irradiation to which he has been subjected.

A Case for Diagnosis. Presented by Dr. Joseph A. Luhan for Dr. Sigmund Krumholz.

A married woman, aged 32, of Polish descent, was admitted to the Cook County Hospital on April 12, 1934, complaining of severe numbness and inability to recognize objects in the left hand, numbness of the body from the breasts down and difficulty in walking. Fourteen years ago, when 18 years of age, the patient noticed that she had burned a finger on the left hand without experiencing pain. Following this she dropped objects held in the left hand because she had no feeling for them. If she watched her hands she was able to hold things. This condition persisted for about eight months, when gradually perfect recovery ensued. The patient remained well until two years ago, when she began rather suddenly to bleed from the nose and mouth, and blood was present in the stools and urine following the taking of some bromoquinine. Chills and vomiting were also present. This condition lasted for three weeks. Subsequently it was determined that taking bromoquinine provoked a similar attack.

The present nervous symptoms (coming on after a lapse of fourteen years during which there were no noteworthy subjective complaints referable to the nervous system) began three weeks before the patient was admitted to the hospital (about two months ago), when she awakened one morning to find the left upper extremity numb and experienced needle prick-like sensations in the tips of the fingers. She could not recognize objects held in the left hand by means of touch and dropped things unless she watched them.

A week later there was similar numbness in the body from the breasts down, and a tingling sensation was present in the toes. Walking was difficult because the patient was unaware of the exact position of the lower extremities. A week later she observed that the right hand was numb. At about this time she noticed that once the act of defecation was initiated she had little control over the sphincter and the normal sensation associated with the act was lost.

Examination at the time of admission revealed: marked ataxia in the left upper extremity during the finger-to-nose test, slight ataxia in the right upper extremity and considerable ataxia in the heel-to-knee test. The position sense of the digits was much impaired in the left hand, and less so in both feet. There was stereoanesthesia in the left hand. The touch sense was impaired in the left hand and over the left breast; the pain and the temperature sense were everywhere preserved. The knee and achilles tendon jerks were exaggerated on the left, and a Babinski sign was elicited on that side. The cerebrospinal fluid showed: Pandy test, 3+; cell count, 360 lymphocytes; Wassermann reaction, negative, and colloidal gold curve, 1111100000. The Wassermann reaction of the blood was negative. Gastric analysis showed: free acidity, 0; combined acidity, 31 degrees. The red blood cell

count was 5,400,000; with 101 per cent hemoglobin; white blood cell count was 10,950, with 70 per cent polymorphonuclear neutrophils. A subsequent spinal puncture revealed only 49 cells. The spleen was definitely palpable.

Examination today (May 19) reveals essentially the same findings as were noted at the time of admission except that the stereo-anesthesia and loss of joint sense in the left upper extremity are profound. Similar findings, of milder grade, have appeared in the right upper extremity. Vibratory sensibility is only moderately diminished in the left upper extremity and is elsewhere fairly normal. The patient has regained ability to walk and shows scarcely any ataxia in the lower extremities. Neither plantar reflex is elicitable, and no pathologic reflexes are present. There has been no history of precipitate micturition. The subjective complaint with respect to the act of defecation has disappeared. The ocular fundi appear normal.

DISCUSSION

DR. PETER BASSOE: Has this patient had polycythemia at any time? This should be considered because it may produce peculiar symptoms.

DR. PERCIVAL BAILEY: Some doubt was cast on the findings in the spinal fluid in the beginning, but it is possible that there were 360 lymphocytes in the fluid at the time the first puncture was made. There have been many cases in which there were large numbers of lymphocytes in the fluid with nothing found to account for them. A patient of mine had over 400 cells, which number decreased gradually in the course of a month until finally there were 49. The patient recovered, and I have no idea to what it was due. Such cases have been described elsewhere as instances of simple lymphocytic meningitis.

CARBOHYDRATE METABOLISM: THE EFFECT OF HYPOTHALAMIC LESIONS AND STIMULATION OF THE AUTONOMIC NERVOUS SYSTEM. DR. LOYAL DAVIS, DR. DAVID A. CLEVELAND and DR. WALTER R. INGRAM.

This article will be published in full in a later issue of the ARCHIVES.

DISCUSSION

DR. LOYAL DAVIS: The question of the control of carbohydrate metabolism is not simple; all the glands of internal secretion are involved in one way or another. This article is not an attempt to settle the question. We have simply presented data on a series of animals to show that a lesion properly placed in the hypothalamus will control diabetes that follows removal of the pancreas. We have not transplanted the pituitary gland, as did Barnes, and produced hyperglycemia and glycosuria. We realize that the hypophysis has a nerve and blood supply which may be injured in these lesions and may give some of the results we have obtained.

The other part of our problem is a corroboration of the work of Cushing. Carlson attempted to corroborate the work of Cushing, Weed and Jacobson but failed to produce glycosuria. The fact was that they did not always have animals in which glycogen was available. It is certainly of interest that a hypothalamic lesion may prevent the production of glycosuria and hyperglycemia following lesions of the pancreas and stimulation of the superior cervical ganglion.

DR. WALTER R. INGRAM: There are many different terminologies for the different nuclear groups of the hypothalamus. I think that the best terminology is that used by the Michigan school, which we have attempted to follow in our work. Relatively slight differences in lesions will produce rather markedly different effects. In 60 or 70 experiments in collaboration with Dr. Ranson and Dr. Fisher, in which we have placed lesions in the hypothalamus, we have been surprised at the scarcity of visible symptoms. We expected to find marked obesity in our animals but have not been able to obtain definite results in this respect. In lesions that produced atrophy of the posterior lobe there was possibly a slight increase of weight when the cat was on a constant maintenance diet. Cats on an

unlimited diet gained weight, but normal animals gained as much as or more than the animals that had been operated on. Operations which interrupted the tractus hypophyseus produced diabetes insipidus similar to that occurring in man. In these animals we found atrophy of the posterior lobe of the pituitary gland. In 5 or 6 cats the polyuria persisted for several months; this study is still going on.

In regard to carbohydrate metabolism, we have made hundreds of studies of the blood sugar and have been unable to convince ourselves that any marked or consistent change results from the lesions. There are many inconsistencies in the literature in relation to the hypothalamus and carbohydrate metabolism. Some workers have reported a rise in blood sugar from stimulation of the hypothalamus. Ranson and others found such a rise, as did workers in Japan. Miki claimed that stimulation of the paraventricular or filiform nucleus caused a rise in the blood sugar level and that destruction of this cell group produced a fall. Morgan, Vonderake and Malone claimed to have found degenerative changes in the paraventricular nucleus in cases of diabetes mellitus in man, but this does not fit in with the results of Miki's work. In a number of cats with lesions placed in the caudal portions of the hypothalamus we have found very high blood sugar, which apparently responded to insulin. At least one of these animals showed a diabetic type of respiratory quotient. There is a possibility that these effects may have been due to irritation of the anterior lobe of the pituitary.

Dr. David A. Cleveland: It is true that Cushing obtained glycosuria following removal of the splanchnic nerves. In 3 cats of our series in which the splanchnic nerves were cut we did not find glycosuria. I think this fact needs much more study, and possibly later we can explain it. All the cats were well fed, and the question of diet did not enter in. They were not under a diabetic control but were fed a standard diet; if they did not eat they were fed by tube.

The Relation of Recovery of Different Sensory Branches of Peripheral Nerves to Recovery of Motor Function. Dr. Lewis J. Pollock.

One hundred and sixty-seven records of sensory regeneration in nerves following injury have been analyzed to determine any possible relation between the recovery of motor function in certain muscles innervated by injured nerves and sensory regeneration in particular sensory cutaneous branches. Sensory regeneration did not appear to be coextensive with recovery of the motor function in the ulnar nerve, occurring in only 50 per cent of cases. There was no specific relation between the return of sensation in individual nerves and the recovery of motor function in certain muscles. When motor function was returning in the median nerve following injury, sensory regeneration could be demonstrated in 63 per cent of cases and overlap in the rest. No relation was found between the return of sensation and the recovery of function in individual muscles. In most cases of injury of both the ulnar and the median nerve, sensory loss in the median nerve was incomplete in about 88 per cent of cases, and in the ulnar nerve, in only 23 per cent.

In 80 per cent of cases the recovering radial nerve showed sensory regeneration; it was found in a greater proportion of cases in which regeneration was found in the extensor pollicis longus and extensor digitorum communis muscles than in cases in which the extensor muscles of the wrist were recovering.

The more muscles recovering in cases of lesions of the peroneal nerve, the more patients showed sensory regeneration of the sural nerve. The musculocutaneous and anterior tibial nerves showed sensory regeneration in only 26 per cent of all cases, in this way corresponding to the ulnar nerve. No correlation was found between recovery of sensory and that of motor function.

In cases of injury of the sciatic nerve, recovery of motor function of the peroneal nerve is associated more frequently with sensory regeneration in the musculocutaneous and anterior tibial nerves than in cases of isolated lesions of the peroneal nerve, and sensory regeneration is related somewhat to recovery of motor function in the extensor digitorum communis and extensor hallucis muscles.

In some cases in which the tibial nerve was completely paralyzed, marked sensory regeneration was found, and in other cases in which complete recovery of motor function was present no recovery of sensation was found.

Complete recovery of sensation in the tibial and peroneal nerves was found in cases in which there was partial recovery of motor function. Complete recovery of sensation in either the tibial or the peroneal nerve was found when there was incomplete recovery of motor function, indicating a gross intraneural localization.

SOME USES OF INSULIN IN PSYCHIATRY. MERLE Q. HOWARD, Wauwatosa, Wis. (by invitation).

Insulin has been used as an agent to stimulate the appetite and digestive mechanism in general of undernourished psychotic patients at the Milwaukee Sanitarium. The majority of the patients treated had some one of the various types of depression. Some patients with organic psychoses and psychoneuroses were included in the group. Part of the regimen employed was to determine first the ideal weight of the patient. From this the normal necessary food intake in calories was estimated by multiplying the ideal weight in pounds by 16. An arbitrary dose of 10 units was given at first; this was increased or decreased as indicated by the response. It was found that all patients so treated responded well, particularly those who were depressed.

Insulin has been used also in the treatment of patients with drug addiction. It was given first for tonic purposes, and it was found that these patients had a more comfortable convalescence than usual; insulin was then adopted as a means to facilitate the withdrawal of morphine in cases of addiction. Patients so treated recovered from the withdrawal with a minimum amount of discomfort and in a relatively short time. From certain observations it was deduced that the continued use of morphine created certain changes in carbohydrate metabolism, for which the body made gradual compensation. When the drug is suddenly withdrawn, symptoms arise as a result of disturbance of this compensation, together with acidosis. While this conclusion is largely empirical, certain investigations tend to bear out the hypothesis. It has been shown that the continued use of morphine has an influence on the acid-base equilibrium and also that a certain parallelism exists between a rise in the blood sugar and the reaction of the blood. A rise in blood sugar following the injection of morphine has been noted and is believed to be due to an excessive secretion of epinephrine, causing decomposition of glycogen in the liver and conditioning in this manner a rise of blood sugar. Other observers have found, following removal of the suprarenals in animals, that a rise of blood sugar fails to appear after the administration of morphine. It has also been found that hyperglycemia fails to appear after section of the splanchnic nerves, indicating that morphine stimulates the sympathetic nervous system and brings about mobilization of epinephrine, the results of which are expressed in a rise of blood sugar. Other observations were a rise in blood sugar following the withdrawal of morphine in animals accustomed to repeated injections of the drug, and the discovery of a negative water balance in morphine addicts from whom the drug had been withdrawn.

One German author decided that blood sugar curves for morphine addicts point to a disturbance of utilization of grape sugar and therefore a functional disturbance of the liver. He reported the results of treatment of 3 patients with insulin and grape sugar; there was a decrease or absence of the manifestation of abstinence with a remarkably rapid return of euphoria and psychic equilibrium.

I have treated 10 patients successfully with the following regimen. Insulin was not substituted for morphine immediately if the patient had been taking more than 3 grains (0.195 Gm.) a day or if the physical condition of the patient was not good. In the former instance the dose was gradually reduced to 2 grains (0.13 Gm.) a day, and then insulin was substituted for morphine. In the latter case morphine was administered in sufficient doses to maintain comfort until the physical condition was such that insulin could be given safely. When sedative or hypnotic

medication was necessary, barbiturates were given. The carbohydrate in the diet was kept at a high level, as were fruit juices and sugar. The dose of insulin varied with every patient, but the amount given was that which gave the most relief. As much as 120 units was given in a day, with no serious lowering of the blood sugar. The substitution of insulin was first started when symptoms appeared following the withdrawal of morphine, and the dose could then be determined fairly well. The duration of its use depended on the time in which the patient was able to make an adjustment. In all the patients treated I have found an absence or a minimum of symptoms following withdrawal of insulin.

PSYCHOLOGIC FACTORS IN THE ETIOLOGY OF DIABETES. DR. WILLIAM C. MENNINGER, Topeka, Kan. (by invitation).

A study has been made of 22 cases of mental disorder associated with diabetes; in 10 cases the diabetes and mental disorder developed together; in 5 the diabetes developed in the course of the mental disorder, and in 7 the diabetic condition was established and known before the onset of the mental symptoms. In 5 of the cases studied the metabolic disorder appears to have been initiated by the psychologic conflict and to have run a parallel course with the mental illness. The criteria for the selection of these 5 cases were: (1) Obvious psychopathology was evidenced prior to the development of the glycosuria; (2) the mental picture was different from the toxic state occasionally seen in cases of hyperglycemia or hypoglycemia; (3) the course of improvement in the mental picture was paralleled by the levels of sugar in the blood and urine, with fluctuations in these as emotional upsets occurred in the psychic life; (4) the metabolic disorder was indicated by a persistent glycosuria, retarded dextrose utilization curves of the blood sugar and a response to dietary and in some cases to insulin therapy; (5) with mental recovery, the diabetic condition disappeared, requiring neither insulin nor rigid dietary treatment.

It is concluded that psychologic influences may initiate diabetes as well as greatly influence the course of an established diabetic condition. Further, in the light of information gained from psychiatry, and in particular from psychoanalysis, it is suggested that the powerful influences of unconscious conflicts may be responsible for the causation of a diabetic state in some instances.

DISCUSSION

DR. THOMAS L. FENTRESS: In my opinion the principal objection to any discussion of the psychogenic factors in the etiology of diabetes is the failure to distinguish between anxiety and other emotions. During the past two years Dr. Alfred Solomon and I have been working at St. Luke's Hospital on the physiologic changes which occur in emotion. We have found that patients with anxiety states show such parasympathetic phenomena as a low basal metabolic rate, hypotension, hypoglycemia, secondary anemia, irritability of the colon, etc. In other words, I cannot see how anxiety can cause hyperglycemia. On the other hand, the essayist spoke of one patient who had persecutory delusions of an obviously sadistic nature, and I can understand how an emotional reaction at a sadistic level might produce hyperglycemia. It used to be said that when the stock market went down the blood sugar went up. That is not a fear reaction, but a rage reaction. I cannot believe that men in love show hyperglycemia. I think they have a low blood sugar.

DR. PERCIVAL BAILEY: I wish also to make a distinction. The author spoke about a contradiction between the frequency with which physicians admitted that diabetes was aggravated by emotional upsets and their apparent reluctance to admit the psychogenic causation of diabetes; I see no contradiction there. That a person with diabetes is worse during emotional strain is a fact of observation which may be verified and apparently has been by many physicians. But that diabetes may be caused by emotional stress is an inference, and all inferences from observed fact must be drawn with due caution, as age-long experience has taught.

Dr. Lewis J. Pollock: Although I have been trained in the era of organic neurology, during this training I have felt that it was necessary always to evaluate psychogenic factors in the production of disease. The road of science is arduous and long, and short cuts, I think, lead largely to disbelief. When Dr. Menninger says that there is evidence that psychogenic conditions may influence diabetes mellitus I am in agreement with him; when he says that psychogenic conditions may be responsible for it I am willing to keep an open mind and watch for developments, but when he says that they cause diabetes mellitus I am not in agreement. It is necessary to define not only the psychologic but also the physical. The diagnosis of diabetes mellitus is dependent not alone on the sugar curve but on many other factors. The influence of psychogenic factors on the development of diabetes is nothing new. Dejerine pointed out defects of function of practically all organs which were brought about by psychogenic factors. Many patients if vexed would die of angina pectoris. Rupture of the vessels of the brain, gastric ulcer, spasm of the pylorus, mucous colitis, polyuria, polydipsia, tachycardia, bronchiole spasm, asthma, allergy, thyrotoxicosis, epilepsy and parkinsonism—in fact, all conditions in the body—are associated with psychogenic factors, yet they need not be the results of such factors alone.

The point of my discussion is this: I favor in every respect and support all investigation leading to a careful consideration of psychogenic factors, not particularly in the conscious or the unconscious, in the production of disease, but before it is stated that defect of a physiologic function is the result of a psychogenic factor alone one must have proof from histologic and careful postmortem examinations.

Dr. William C. Menninger: First, I tried to point out that I do not assume that diabetes is associated directly with anxiety. One cannot be sure about this point, but the best proof is that emotionally disturbed psychotic patients show glycosuria in only a few instances. My second point is in support of what Dr. Pollock has said. I have tried to be conservative, and I carefully avoided stating in my conclusions that diabetes is caused by emotional factors. It may be, but in any event I am sure that the emotional factors may initiate diabetes. The emotional factors start a train of physiologic function which ends in the clinical picture of diabetes. Dr. Pollock made a point which I can best criticize myself. It might have been wiser, in view of the unsettled knowledge of the physiology of diabetes, to use the term disorder of carbohydrate metabolism. This was Dr. Solomon Strouse's criticism of this paper, and he is much interested in this special field. Through his kindness, I have been interviewing diabetic patents at the clinic of the Michael Reese Hospital with a psychiatric approach; all that I have seen supports my conclusions in this paper. I am sure that the emotional factors are important, not only in the etiology but also in the control and management of diabetes.

Book Reviews

Gehirn-Pathologie vornehmlich auf Grund der Kriegserfahrungen. By Karl Kleist. Price, 122 marks. Pp. 1,065, with 419 illustrations. Leipzig: Johann Ambrosius Barth, 1934.

Kleist's volume on the pathology of the brain is the most extensive recent work on the subject and is second only to Henschen's "Klinische und anatomische Beiträge zur Pathologie des Gehirns" as a source book for case material. Almost all the cases, numbering about two hundred and eighty, are those of patients whom Kleist saw during the World War, but the nature of the disorders and the pathologic observations in these cases, in which the injuries were chiefly cortical, are considered in relation to the conditions which Kleist or other investigators saw in civil practice.

The first sections of the book are on motor and sensory disorders. They are followed by chapters on apraxia and visual and auditory disorders and a long discussion of the aphasias. The final sections cover disorders resulting from lesions of the frontal lobe and of the basal ganglia.

The system which Kleist presents throughout is that of the protagonist of extreme cerebral localization. Disorders are subdivided into a series of distinct types, for each of which Kleist seeks a specific pathologic condition of the brain. The chief subdivisions that he makes and the functions that he allocates to the various cerebral areas may be quickly surveyed by inspection of the diagrams in the concluding section. Diagrams of the basal ganglia and the upper part of the brain stem are given in an earlier part of the book, and in these not only myostatic but also psychokinetic and catatonic disorders are localized in specific areas.

The extent of the cerebral differentiation which Kleist admits may be illustrated by reference to his discussion of motor amusia. He distinguishes, in addition to "melody muteness," a new form which he calls "tone muteness." The basis for the differentiation for pure tone muteness is one of the cases during the World War; the patient could hum a melody correctly but could neither sing nor whistle a note. The localization of the motor center for tone formation is said to be the foot of the anterior central convolution, "which can be divided into a whistling center lying higher up and a singing center lying underneath."

The divisions of apraxia which Kleist outlines are four: limb kinetic, idiokinetic, constructive and ideational. The first, second and fourth are essentially the types which Liepmann differentiated, although Kleist differs from Liepmann on certain points; for example, he denies that there is any dyspraxia on the left side with limb kinetic apraxia of the right hand. The third, the constructive apraxia, is the disorder which Kleist himself first described and which has been studied so much recently in connection with disturbances of "spatial thought."

The divisions of aphasia are those which Kleist outlined in his earlier articles on the basis of the material seen in the World War, and his concepts of aphasia are apparently unchanged. He distinguishes two main groups, the sensory and the motor, and four principal types within each of these groups. The four sensory and the four motor divisions are parallel and apparently represent a logical analysis of the speech process. They are: first, sound deafness and sound muteness, the simplest or so-called pure aphasic disorders; second, word deafness and word muteness; third, sentence deafness (paragrammatism) and sentence muteness (agrammatism), and, fourth, word-sense deafness, or amnesic aphasia, and name muteness. Careful reading of the records of cases in this section, as well as in all the other sections dealing with psychic disorders, shows studies which are usually satisfactory from the clinical standpoint and admirable from the pathologic standpoint, but almost always inadequate as studies of mental processes. In part, this

serious difficulty is, of course, a natural result of the hasty studies which had to be made under the pressure of war conditions, but in part it reflects Kleist's dominant interest in cerebral localization.

It is the structural rather than the dynamic point of view which is manifest throughout the book, and this statement holds in spite of the fact that there are occasional references to dynamic concepts by way of explanation. Kapper's law of neurobiotaxis is, for example, introduced to support the localization of color agnosia. Kleist notes that the color image has two associations, one to the image of the colored object and the other to the name of the color. The object belongs to the extended visual sphere, the name to the nearby part of the temporal lobe. According to Kapper's law, the nervous structures develop in the direction of the strongest stimuli; in this instance the nervous bases for the color images, for which speech stimuli are stronger than any others, develop toward the temporal lobe, the area where names are located.

In the scope of any review it is impossible to touch on more than a few of the many topics of the book, all of which are presented with valuable case material and critical discussion. They will require the careful attention of all students of brain organization. Many will, however, disagree with Kleist's interpretation of the findings, thinking it better to study the complex functional relationships within the disorder than to divide it into a series of isolated phenomena, and better to concentrate on the problems of cerebral functioning than on the differentiation of specific cerebral areas.

Unfall und Hirngeschwulst. By O. Marburg. Price, 8.80 marks. Pp. 106, with 12 illustrations. Vienna: Julius Springer, 1934.

In this short monograph Marburg attempts to establish the connection between cranial trauma and some types of tumor of the brain. Analysis of previous reports leads him to conclude that tumors may arise by trauma. It is of interest that the rôle of trauma was considered more important among the older neurologists than among those of the present day. To quote a few statistics: Gerhard found that 17 per cent of gliomas originate through trauma. Müller reported the incidence of trauma in tumors of the frontal lobe to be 18.7 per cent. Monakow found a history of trauma of the head in thirty of one hundred patients with tumor of the brain, and in ten of these he could establish that the trauma served as the impetus to the tumor formation. Oppenheim believed that trauma can serve as the impetus to the formation of some tumors. Kinnier Wilson, on the other hand, believed that brain tumor formation has no relation to trauma, because there was no increase in the incidence of tumors in the war.

The possibility of the development of tumor of the brain as a result of trauma has always been conceded, but the number of such cases is small. There are certain fundamentals which must be fulfilled in order to establish the relation of tumor of the brain to trauma: (1) There must have been good health before the trauma; (2) the trauma must have been severe, without necessarily being followed by loss of consciousness; (3) there must have been a latent period after the trauma (which may vary greatly, being possibly very short for blastomatous tumors) and the location of the growth is important, and (4) the closer the glioma is to the primary seat of the trauma the more likely there is to be a direct relationship between the two.

From a survey of the literature and from his own experience, Marburg found that trauma seems to have played some rôle in the following types of tumors: (1) gliomas, in four cases; (2) neurinomas, in twenty; (3) meningiomas, in thirteen; (4) angiomas, in four; (5) sarcomas, in fourteen; (6) granulomas, in five, and (7) cysticercus cyst, in three. He concludes from his study that all types of tumor of the brain may at one time or another be conditioned by trauma. There is no form of glioma which may not be so conditioned, and of the various types the glioblastoma multiforme appears to be the one most frequently associated with trauma. The more severe the trauma the more likely it is to be associated with tumor. Reports of minor traumas are not infrequently encountered in the

histories, however. One of the most important arguments for the association of trauma and tumor of the brain is that such tumors develop in the immediate vicinity of the trauma. Another argument is to the effect that some tumors of the brain develop around foreign bodies which have been introduced by the trauma.

Marburg has succeeded in marshaling many cases of tumor which are related in some way to trauma, but the cause and effect relationship of trauma to tumor is still unconvincing. The fact that a tumor develops under the seat of a trauma is not in itself proof that it caused the tumor to develop. Who is in a position to state that the tumor was not present before the trauma, particularly since slowly growing tumors may develop in some parts of the brain without giving evidence of their presence? More convincing are the cases of tumor which develop around foreign bodies in the brain. In the case of gliomas, symptoms may develop either soon or late after trauma. In the former case it is more than likely that trauma has merely precipitated symptoms by the occurrence of hemorrhage in the tumor or by causing a sudden expansion of a mass which had previously given little evidence of its presence. In slowly growing tumors, despite the development of a mass under the seat of the trauma, the time relation of the trauma to tumor is so indefinite as to make the evidence at best unconvincing.

If one accepts the principles laid down by Marburg for establishing the relationship of trauma to tumor of the brain, one is immediately in difficulties. The first principle—that the patient must have been previously in good health—is not in itself a safe guide, for slowly growing tumors, such as astrocytomas, may exist in the brain for some time without causing symptoms. The second principle—that the trauma must have been severe—is not always true, for not infrequently it is a minor one. Moreover, there is always the possibility that the trauma may be the result rather than the cause of the tumor, brought about because of symptoms, such as vertigo, due to the tumor.

Trauma has been assigned a place of importance in some cases of meningioma. Spiller has maintained for many years that trauma may be followed by hyperostosis and, later, by the development of an underlying meningioma.

The study is valuable because it brings together all the available evidence that trauma is a cause of tumor. The subject is extremely important from the medicolegal standpoint. It is important, moreover, to consider the causes of tumor of the brain, and Marburg's study represents a valuable contribution in this direction. The monograph is clear and concise and is highly recommended to neurologists and neurosurgeons.

Russia, Youth and the Present-Day World: Further Studies in Mental Hygiene. By Frankwood E. Williams. Price, $2.50. Pp. 270, with 31 illustrations. New York: Farrar & Rinehart, 1934.

The papers and addresses collected in this book are not studies in mental hygiene in a limited sense, but discussions of the changes in social organization which are consequent on the Soviet philosophy and social aim. These changes involve a new concept of mental hygiene, just as they involve a new concept of education and of the relation of the worker to the social organization. Dr. Williams became convinced, as a result of his recent visit to Russia, that the psychiatrist there sees as his primary function not the treatment of persons who have become ill or maladjusted but the arrangement of conditions in the school, factory and every other center so as to build up the mental health of all the persons in the group. Instead of thinking in terms of the 10 or 15 per cent of the population which is in difficulty, he thinks in terms of 100 per cent of the population and is able to work toward health for the masses because all the organizations within the social structure are also working toward the same goal. Dr. Williams' conviction makes his book stimulating, and even those who believe that he paints too dark a picture of education and family relationships in the United States must nevertheless be challenged by the success which he reports for many of the Russian systems and the even greater success which he foresees for them.

Syllabus of Psychiatry: A Guide to General Orientation. By Leland E. Hinsie, M.D., Professor of Clinical Psychiatry, Columbia University College of Physicians and Surgeons. Price, $2.50. Pp. 348. Utica, N. Y.: State Hospitals Press, 1933.

This is an unusual book so far as its similarity to the ordinary type of psychiatric publication is concerned. The material was based on a lecture course given as part of the graduate courses in neurology and psychiatry at Columbia University. It was the intention of Hinsie not to build a text but to correlate material found in various psychiatric books. As a supplement to textbook study the book will furnish a good reference work for graduate students. It is not all-inclusive but presents certain aspects of psychiatry in a new and interesting manner. The book is divided into five chapters: I, "Constitutional Concepts"; II, "Psychical Concepts"; III, "Psycho-physical Concepts"; IV, "Sociological Considerations," and V, "Endogeny and Exogeny."

This is not a text for undergraduate students. It has value for workers in fields other than psychiatric medicine, for in the section on sociologic considerations much emphasis is placed on the relation of the clinical syndromes to the environment as a whole. The work is an interesting departure from the cut and dried form of textbook psychiatry and may stimulate further writings along these more special lines.

Civilized Life: The Principles and Applications of Social Psychology. By Knight Dunlap. Price, $4. Pp. 374. Baltimore: Williams & Wilkins Company, 1934.

In this book Dunlap has incorporated the material of his "Social Psychology" and added several new chapters. The subject touches on many different fields—anthropology, religion, social and political organization, marriage and the family. The material in all these fields is presented dogmatically in an effort to stimulate opposition and controversy. The book will be of considerable interest to the psychologist or the sociologist, but of less interest to the psychiatrist.